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The American Heart Journal

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The American Heart Journal

VOL. 10 APRIL, 1935 NO. 4

Original Communications

ASYNCHRONISM IN CONTRACTION OF THE VENTRICLES IN THE SO-CALLED COMMON TYPE OF BUNDLE-BRANCH BLOCK: ITS BEARING ON THE DETERMINATION OF THE SIDE OF THE SIGNIFICANT LESION AND ON THE MECHANISM OF SPLIT FIRST AND SECOND HEART SOUNDS*†

CHARLES C. WOLFERTH, M.D., AND ALEXANDER MARGOLIES, M.D.
PHILADELPHIA, PA.

THE views of Eppinger and Rothberger[2] and Lewis[3] regarding the electrocardiographic localization of the side of the significant lesion in bundle-branch block, which were based on animal experimentation, have not been universally accepted as applicable to man.[4, 5, 6] The opponents of these views have pointed out that the different anatomical relations in man as compared with dogs render unsafe generalizations regarding the conducting apparatus in man from data obtained in dogs. The evidence resulting from serial sections of the A-V conduction system in cases which had exhibited bundle-branch defects is apparently conflicting.[7-11] There are, however, very few cases reported in which (1) the electrocardiograms conform strictly to the criteria of bundle-branch block, and (2) histological studies are adequate. The data obtained by (a) experimental production of extrasystoles in man,[12] and (b) studies on the order of ventricular excitation in bundle-branch block by the use of semidirect leads[6] have led Wilson and his coworkers to conclusions directly opposite to those of Eppinger, Rothberger and Lewis. Recently, doubt has been cast on the validity of the conclusions of Wilson and his group by Katz and Ackerman,[13] who have demonstrated in dogs the importance of comparatively slight changes of position of the heart on the direction of

*Presented in part before the Association of American Physicians, May 9, 1933.[1]

†From the Robinette Foundation, Medical Division, Hospital of the University of Pennsylvania.

the QRS complex. These observers believe that it is unjustifiable to attempt to localize the site of the bundle-branch block from the direction of the major initial complex of the three leads of the electrocardiogram.

It is desirable for the development of our knowledge of electrocardiographic localization of myocardial damage, that the side of the lesion in the common type of bundle-branch block be determined beyond doubt. It occurred to us that new evidence bearing on the problem might be obtained by studying the time relations of various phenomena related to ventricular contraction on the two sides of the heart. The hypothesis that asynchronism in contraction of the two ventricles may occur is not new.* Before the advent of electrocardiography, some writers maintained that reduplication of the first sound is due to asynchronism in the beginning of contraction of the two ventricles. This idea has received little, if any, support in recent years,

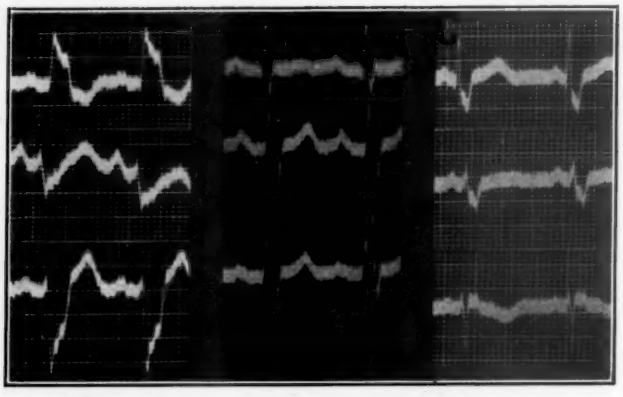

Fig. 1.—*A*, The common type of bundle-branch block.

B, Case J. O'C. (Table IV). A relatively uncommon type of intraventricular conduction defect.

C, Case A. O. (Table IV). This type of intraventricular conduction defect ranks second in frequency to the common type. The significant lesion probably involves the conduction system on the right side.

although no actual evidence opposed to it has been presented. As far as we know, it has never been tested in man. Most clinicians probably believe that reduplication of the second heart sound is due to asynchronous closure of the aortic and pulmonic valves, but no adequate proof has been available.

Katz[15] has shown in experimental animals that there is often slight asynchronism in the beginning and ending of the ejection periods from the two ventricles. The frequency with which splitting of both first and second heart sounds is noted in bundle-branch block and the reported finding of a bifid systolic apex impulse[16] suggest that these phenomena might be due to asynchronous contraction of the

*This subject has been reviewed by Holt.[14]

two ventricles. Moreover, such a hypothesis seems reasonable, because, according to the generally accepted explanation for the mechanism of bundle-branch block, the excitatory process is delayed in reaching the ventricle on the side of the block. The response might therefore also be delayed.

In the present study, the time relations of various events associated with right and left ventricular contraction were studied in a series of patients, whose electrocardiograms conformed rigidly to accepted criteria for the so-called common type of bundle-branch block (Fig. 1*A*).

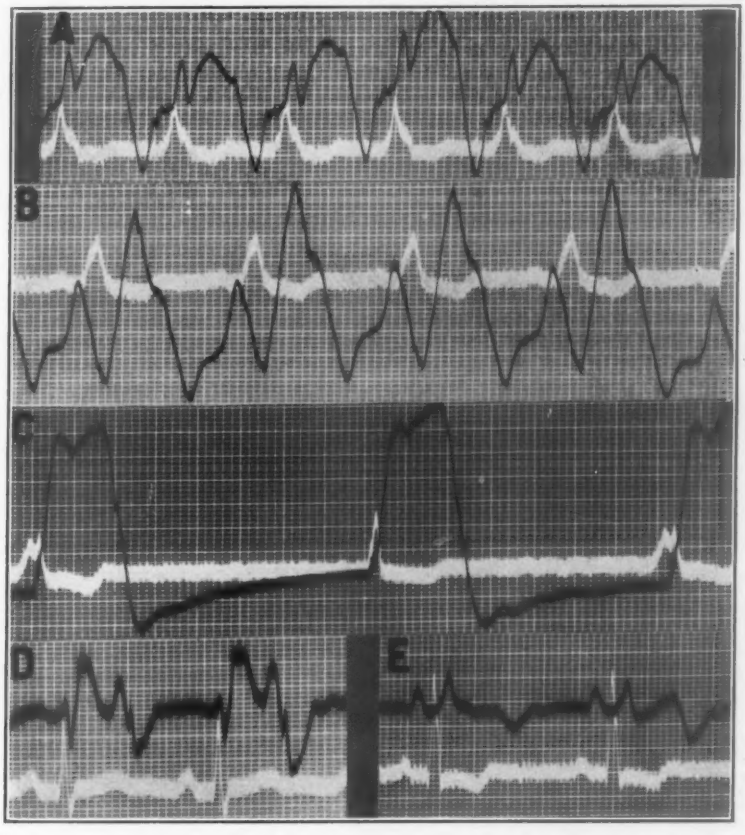

Fig. 2.—Various types of apex impulse in cases with bundle-branch block and cases without bundle-branch block.

A, Case R. B. (Table 1). Bifid apex impulse in the common type of bundle-branch block, both components beginning during the period of ventricular systole.

B, Case R. J. Bifid apex impulse in the common type of bundle-branch block, one component beginning before and one during ventricular systole.

C, Case H.H. (Table I). Single apex impulse in the common type of bundle-branch block (first and third beats). The second beat illustrates the occasional recovery from bundle-branch block which occurred in this patient. While the contour of the apex impulse is similar in both types of beats, its onset is considerably retarded in the beats showing bundle-branch block.

D, Bifid apex impulse in a patient with normal intraventricular conduction time. Both components occur during ventricular systole.

E, Bifid apex impulse in a patient with normal intraventricular conduction time. The first component of the bifid impulse precedes ventricular systole.

All the cases in this series, so classified, had the following electrocardiographic characteristics: (1) the QRS complexes had a duration of not less than 0.14 of a second in at least one lead; the amplitude of the QRS complex in Lead I was at least 6 mm. and in Lead III was always greater; (2) the main QRS complex was upward in Lead I and downward in Lead III; (3) the terminal or T-deflection was downward in Lead I and upward in Lead III.

The methods used for determining the various time relations under consideration included (1) various combinations of electrocardiograms, sound tracings,* optically recorded apex cardiograms, carotid artery and venous pulse tracings with the recording devices arranged to avoid parallax and (2) roentgenkymographic tracings of the aortic and pulmonary artery pulsations, timed by superimposition of the 60 cycle x-ray current disturbance on an electrocardiogram.

APEX CARDIOGRAMS

Optically recorded apex cardiograms timed by electrocardiograms (care being taken to exclude parallax) were obtained in 5 cases with the common type of bundle-branch block. Three of these cases exhibited a bifid outward thrust in early systole (Fig. 2*A*), one a bifid thrust the first component of which preceded ventricular systole (Fig. 2*B*), and one a single large apex thrust (Fig. 2*C*). The time interval between the beginning of the QRS complex and the beginning of the

TABLE I

TIME INTERVALS BETWEEN THE BEGINNING OF THE QRS COMPLEX OF THE ELECTROCARDIOGRAM AND THE OUTWARD THRUST OF THE OPTICALLY RECORDED APEX IMPULSE

THE COMMON TYPE OF BUNDLE-BRANCH BLOCK		NORMAL INTRAVENTRICULAR CONDUCTION AND GOOD CARDIAC FUNCTION		NORMAL INTRAVENTRICULAR CONDUCTION AND DECOMPENSATION	
CASE	TIME INTERVAL (SECOND)	CASE	TIME INTERVAL (SECOND)	CASE	TIME INTERVAL (SECOND)
W. B.	0.05	E. C.	0.05	K. M.	0.06
H. P.	0.04	F. R.	0.03	H. G.	0.06
R. B.	0.05	P. G.	0.04	L. B.	0.03
L. H.	0.05	S. W.	0.02	W. H.	0.04
H. H.* (auricular fibrillation)	0.05 to 0.08 (During bundle-branch block) and 0.02 (in beats with normal QRS complexes)	K. H.	0.04	A. R.	0.05
		O. G.	0.02	L. Y.	0.04
		A. E.	0.04	W. W.	0.03
		E. M.	0.04	J. G.	0.04
		C. P.	0.03	G. M.	0.06
		J. G.	0.04	A. D.	0.06
Average	0.048		0.035		0.047

*The systolic thrust was single in both types of beats (see Fig. 2 *C*). This case is excluded from the averages because of the presence of auricular fibrillation and consequent variability in duration of intervals between the QRS complex and the beginning of the apex thrust.

*The method of sound recording has been previously described.[25]

outward systolic thrust at the apex was essentially the same in cases of bundle-branch block as in a series of cases with cardiac decompensation. In normal controls the average duration of the interval was slightly less, although the differences could not be regarded as significant (Table I).

A study of the details of apex cardiograms obtained from controls without bundle-branch block, or even intraventricular conduction defect, reveals the fact that some of these cases also have a bifid outward thrust at the apex during systole (Fig. 2*D*). Whether this is a manifestation of asynchronism in some early phase of cardiac contraction cannot be stated at present. The data, although limited, appear to warrant the following statements: (1) A systolic bifid apex impulse is not always recorded in the common type of bundle-branch block; (2) a systolic bifid apex impulse is sometimes recorded in cases without intraventricular conduction defect; therefore (3) a systolic bifid apex impulse is not to be depended on as a sign of bundle-branch block.*

The outward thrust at the apex does not enable one to differentiate, with certainty, movement due to contraction of one or the other ventricle. Furthermore, because of variability in (1) rotation, (2) the relation of the heart to the chest wall, and (3) the duration of the isometric contraction phase, there is no certainty that the outward thrust of the heart has a fixed time relation to either the beginning of contraction or ejection from the ventricles. For these reasons the method was abandoned for the study of our present problem.

THE TIME OF APPEARANCE OF THE PULSE IN THE RIGHT CAROTID

The appearance time of the sharp primary oscillation in the right carotid artery pulse wave offers a fairly accurate criterion for determining the beginning of ejection from the left ventricle.[17] According to reported studies of pulse wave velocity in large arteries, it may be calculated that this primary oscillation begins from 0.015 to 0.025 second after the beginning of ejection from the left ventricle. The measurements of the time intervals between the beginning of the QRS complex and the beginning of the right carotid artery pulse wave in Table II were obtained from tracings in which the electrocardiographic and optically recorded carotid pulse tracings were made simultaneously, care being taken to avoid parallax. The material comprised eleven cases of the common type of bundle-branch block, ten normal controls, and seven cases of cardiac decompensation. Care was taken to include among this group of controls only cases with a single first sound, because of the possibility that splitting of the first sound may be due to asynchronism in some phase of the early part of contraction. Reference to Table II reveals the fact that although

*J. K. Lewis[29] in a study of apex cardiograms in 14 patients with bundle-branch block described them as "normal" in 9, as having a presystolic or protodiastolic impulse in 4, and a double systolic impulse in one.

there was a considerable range in the duration of the interval in control cases, it was significantly prolonged in all cases with the common type of bundle-branch block.* Comparison of the interval in the bundle-branch-block group with the interval in the cardiac decompensation controls, shows that the prolongation of the former cannot be accounted for by feebleness of the heart action. As a matter of fact, most of the patients with bundle-branch block had relatively good compensation and several of them were working.

TABLE II

TIME INTERVAL BETWEEN BEGINNING OF QRS COMPLEX AND BEGINNING OF RIGHT CAROTID ARTERY PULSE WAVE

THE COMMON TYPE OF BUNDLE-BRANCH BLOCK			NORMAL CASES WITH SINGLE FIRST SOUNDS		CASES WITH SINGLE FIRST SOUNDS AND CARDIAC DECOMPENSATION	
CASE	RATE	INTERVAL (SECOND)	RATE	INTERVAL (SECOND)	RATE	INTERVAL (SECOND)
R. J.	75	0.16 (0.13)†	55	0.10	102	0.10
M. R.	80	0.16 (0.13)† (0.20)‡	74	0.10	108	0.13
R. B.	105	0.16	68	0.11	87	0.08
L. H.	80	0.17	61	0.12	105	0.10
H. P.	79	0.16	65	0.09	66	0.12
P. H.	88	0.18	68	0.12	72	0.12
N. S.	50	0.16	82	0.11	74	0.12
E. G.	83	0.21	74	0.12		
E. H.	85	0.16 (0.12 to 0.09)§	75	0.12		
A. N.	77	0.18	60	0.15		
*H. H.	cycle lengths 0.64 to 1.40 second	0.15 to 0.25				
Average	80	0.17	68	0.111	88	0.11

*This case is excluded from the averages because of the presence of auricular fibrillation and varying intervals dependent on preceding cycle length.

†The interval in extrasystoles with QRS deflection downward in Lead I and upward in Lead III.

‡The interval in extrasystoles with main QRS complex upward in Lead I and downward in Lead III.

§During the transition from bundle-branch block to normal type of QRS complex, the QRS-carotid interval shortened.

The duration of the interval between the QRS complex and the carotid pulse in premature beats has special interest. In Case H. H. of the group with bundle-branch block in which auricular fibrillation was also present, the intervals in the premature beats with relatively small pulses were greatly prolonged (up to 0.25 second), whereas the beats falling after the longer pauses had an interval of only 0.15 to 0.17 second (Fig. 3*A*). A small part of the delay in the premature

*Most of these data were included in Table III of the report by Wolferth, Margolies and Bellet.[1] Nichol[18] has recently published similar data on the time relations of the QRS complex of the electrocardiogram and the left subclavian pulse. Although Nichol apparently regards his findings as sufficient for judgment regarding the side of the significant lesion in bundle-branch block, it had not seemed to us safe to do so, even when comparisons with venous pulse tracings were available. Such evidence falls short of proof. It was this conclusion that led us to the attempt to apply the roentgenkymographic method, so that direct measurements of the intervals between the QRS complex and the aortic and pulmonary artery pulses could be made.

beats might be accounted for by lessened pulse wave velocity,* but most of it was probably due to delay in the beginning of ejection. A similar prolongation of the interval was observed in Case M. R. in connection with an extrasystole of supraventricular type (Fig. $3B_2$). However, in this same case the intervals in ventricular extrasystoles

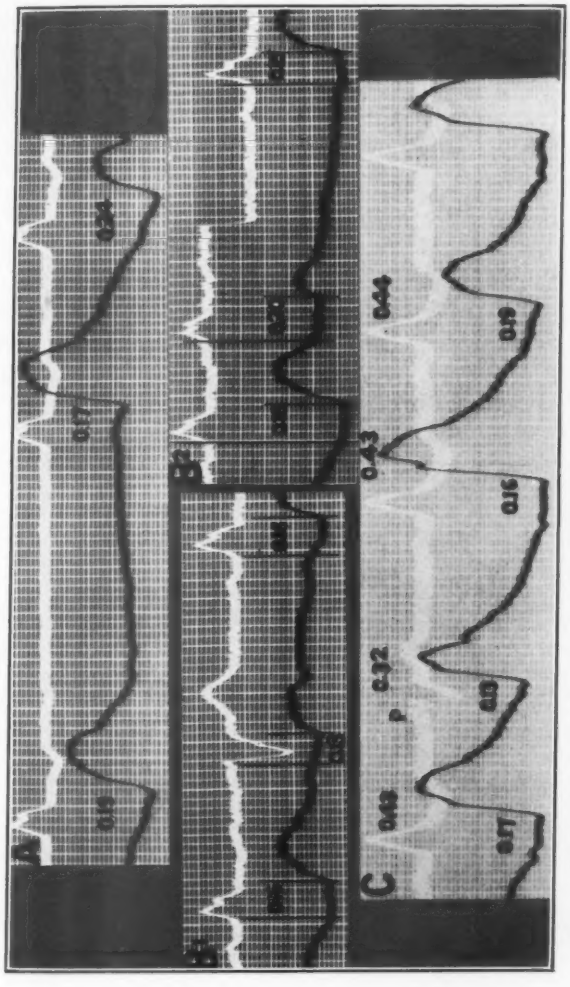

Fig. 3.—Factors influencing the duration of the interval between the beginning of the QRS complex and the upstroke of the carotid pulse in cases with the common type of bundle-branch block.

A, Case H. H. (Table II). Auricular fibrillation. The duration of the diastolic period preceding the beat. The interval is longer in the relatively premature beats.

B-1, Case M. R. (Table II). Extrasystoles with main QRS deflections oppositely directed to that of the common type of bundle-branch block. Despite the prematurity of the beats the interval is shorter.

B-2, Case M. R. (Table II). Extrasystoles with main QRS deflections similar to those of the common type of bundle-branch block. The interval is lengthened in the premature beats.

C, Case R. J. (Table II) illustrates the same phenomenon as *B*-1. The numbers at the top indicate the duration of the interval from the beginning of the QRS complex to the carotid incisura. (See Fig. 9-*A*).

with main QRS deflections opposite in direction to those of the rhythmic bundle-branch-block beats were actually shorter than those of the rhythmic beats, despite the possibly lessened velocity of the feeble premature pulse waves (Fig. $3B_1$). In Case R. J. a similar shortening of the interval was observed in ventricular extrasystolic beats whose

*R. H. Turner, in the discussion of the presentation "Observations on Arterial Function" (R. H. Turner and W. A. Sodeman) before the American Society for Clinical Investigation, April 30, 1934, stated that the velocity of pulse waves in premature beats differed very little from that of normal beats.

main QRS deflections were opposite in direction to those of the rhythmic beats exhibiting bundle-branch block (Fig. 3*C*). Wiggers has found that in left ventricular premature systoles the pressure in the left ventricle rises in advance; in right-sided extrasystoles the right ventricular pressure rise precedes. When this state of affairs exists, from 0.03 to 0.06 second may elapse between the contraction of the two ventricles and asynchronous ejection from the two ventricles takes place.[19]

These observations made on extrasystolic beats appear to indicate that the delay in ejection from the left ventricle in the common type of bundle-branch block is not due to feebleness of the contractions, but is dependent on some special peculiarity in the spread of the impulse which causes a delay in the response of the left ventricle.

The most striking evidence that delayed ejection from the left ventricle is associated with aberrant spread of impulse was obtained in Case E. H. (Table II and Fig. 4). The transition between the common type of bundle-branch block with QRS complexes having a duration of 0.14 second to QRS complexes having a duration of 0.09 second was

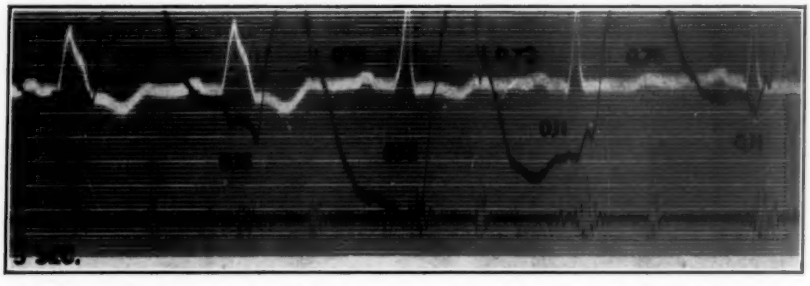

Fig. 4.—Case E. H. (Table II). The effect of transition from the common type of bundle-branch block to normal intraventricular conduction on the interval between the beginning of the QRS complex and the upstroke of the carotid pulse. The interval in the first two beats is 0.16 second, in the third beat 0.12 second, and in the last two beats 0.11 second.

recorded. Coincident with the change in the QRS complexes, the interval between the beginning of the QRS complex and the rise of the carotid pulse changed abruptly from 0.16 to 0.12 and 0.11 second respectively in the two beats following bundle-branch block.

TIME RELATIONS OF THE C-WAVE IN THE VEINS ABOVE THE CLAVICLE

Although the study of the time relations of the carotid pulse demonstrates that ejection from the left ventricle is significantly delayed in the common type of bundle-branch block, it throws no light on the action of the right ventricle. For this reason, the interval between the beginning of the QRS complex and the optically recorded C-wave of the venous pulse just above the right clavicle was measured in a series of 8 cases with the common type of bundle-branch block (7 of which were also included in Table II) and 8 normal controls. The optical apparatus was lined up to avoid parallax. Special care was

taken in the attempt to obtain the venous C-wave (which is most likely dependent on right ventricular activity) and to avoid the arterial C-wave. In the cases having the common type of bundle-branch block, the venous C-wave always fell earlier than the arterial so that the time relations are fairly reliable. In some of the controls, however, there was no certainty that the upstroke of the C-wave was not contributed to or actually caused by the arterial pulse. Nevertheless, the intervals in the cases with bundle-branch block and controls have quite comparable time relations (Table III). It is therefore, justifiable to say that, although in the common type of bundle-branch block the carotid pulse is delayed, the appearance of the venous C-wave in the veins above the right clavicle is not significantly delayed.

TABLE III

TIME INTERVAL FROM BEGINNING OF QRS COMPLEX TO UPSTROKE OF C-WAVE IN THE VEINS ABOVE THE RIGHT CLAVICLE

THE COMMON TYPE OF BUNDLE-BRANCH BLOCK		CASES WITH NORMAL INTRAVENTRICULAR CONDUCTION	
CASE	TIME INTERVAL (SECOND)	CASE	TIME INTERVAL (SECOND)
R. J.	0.12	W. H.	0.10
M. R.	0.12	M. C.	0.10
R. B.	0.13	A. K.	0.09
L. H.	0.11	J. B.	0.11
E. W.	0.10	E. D.	0.12
H. P.	0.12	P. C.	0.09
P. H.	0.14	A. R.	0.06
H. H. (Auricular fibrillation)	0.08 to 0.10	C. T.	0.15
Average	0.116		0.103

While these measurements suggest that in the common type of bundle-branch block ejection from the right ventricle is not delayed, they do not prove the point. The beginning of the venous C-wave does not necessarily bear the same relation to right ventricular ejection as the sharp upstroke of the carotid wave bears to left ventricular ejection. It is quite possible that movement of the heart as a whole may cause a wave to travel up the veins. Furthermore, upward pressure on the tricuspid valve (after closure), which is probably largely responsible for the venous C-wave, may not bear a fixed relationship to ejection. Moreover the velocity of the pulse wave in a low pressure venous system is probably considerably retarded as compared with the velocity in arteries.[20]

ROENTGENKYMOGRAMS OF THE GREAT VESSELS

The procedure of roentgenkymography to record movements of the heart borders was first attempted by Sabat[21] and later by Gött and Rosenthal[22] in 1912. A method of timing the curves by means of electrocardiograms was first used by Becker[23] in 1914 and later by

Stenström and Westermark[24] in 1926. We have recently published roentgenkymographic tracings of movements of the left auricular border in mitral stenosis.[25] The time relations of the roentgenkymograms were analyzed by the use of the superimposed 60 cycle inductive disturbance caused by the x-ray current on the simultaneously recorded electrocardiogram (Fig. 5*D*).

Roentgenkymography of the great vessels does not, as a rule, yield as satisfactory results as that of the heart, since the contrast with the lung fields is not so sharp. This is particularly true of the pulmonary artery region below the aortic knob, because of the adjacent left hilus shadows, which occasionally made kymography of the pulmonary artery difficult, if not impossible. Roentgenkymograms of the aortic knob pulsations were usually obtained without much difficulty. A slit 1.5 mm. in width was used and the film moved past the slit in a motor-driven cassette carrier. Cassette speeds of 3 to 6 cm. per second appeared to be the most satisfactory. The milliamperage varied from 80 to 100 and the kilovoltage from 80 to 100, depending upon the speed with which the cassette was driven and the thickness of the patient's chest. Only those patients in whom satisfactory records of the aortic knob and pulmonary artery pulsations could be obtained were used. Examples of the best results obtained by this technic are shown in Fig. 5 *A*, *B*, and *C*.

The measurement of the time relations involved several possible sources of error. Since the slit was 1.5 mm. in width, there was bound to be slight haziness in the margin of the photographed waves, although this was minimized by the speed with which the film was moved. There was also a hazy band at the beginning and ending of the kymogram. Measurements were made from the middle of these bands. In most of the faster moving films, the slit image was photographed on the moving film by the rectified full wave 60 cycle current impulses as alternate light and dark bands, which could be used as a time signal, the time between successive dark bands being 1/120 sec. (Fig. 5*A*). In the other cases, when it was not distinct enough to be so used, the uniformity of speed with which the film traveled had to be tested by measurements of various time intervals on the electrocardiogram and checked against distances traveled by the film. The superimposed 60 cycle inductive disturbance on the electrocardiogram offered a satisfactory time signal for the duration of the roentgen ray exposure. The amplitude of the disturbance in the electrocardiogram was controlled by means of the so-called induction eliminator, the optimum being a band 3 to 5 mm. wide, so as to obtain a readable electrocardiogram (Fig. 5*D*).

Another factor requiring consideration was the point on the roentgenkymogram marking the arrival of the true arterial pulse wave. In the optically recorded pulse wave there is rarely difficulty in identi-

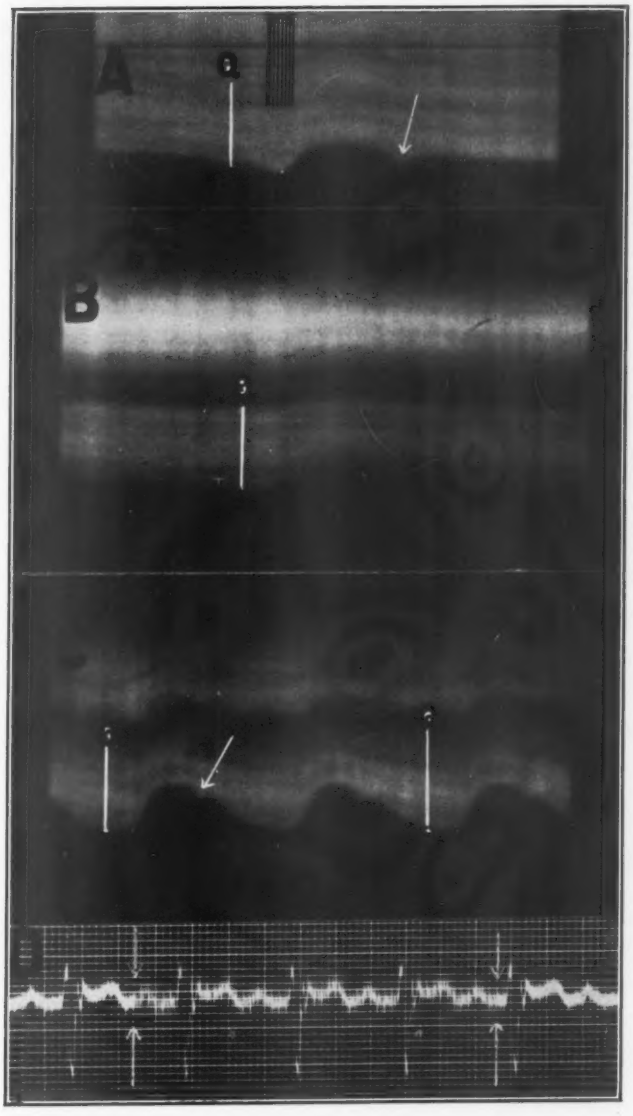

Fig. 5.—Illustration of results obtained in roentgenkymography of the great vessels. The point *Q* in each roentgenkymogram marks the beginning of the QRS complex.

A, A pulmonary artery pulsation. The incisura is distinctly shown (arrow). The alternate light and dark bands (reinforced in part of the photograph for purposes of reproduction) are due to the effect of the rectified full wave 60 cycle current impulses.

B, An aortic pulse wave. The incisura is not distinct in this case although it is in many aortic pulse waves.

C and *D*, Simultaneously recorded roentgenkymogram of the pulmonary artery and electrocardiogram (Lead II) of case J. O'C, (Table IV). The pulse is unusually large, probably due to marked arteriosclerosis in the pulmonary vessels. The incisura is well shown (arrow). The transmission of pulsation to adjacent lung structure is considerable. The beginning and the ending of the inductive disturbance in the electrocardiogram are indicated by the arrows.

fying its beginning. The preliminary waves (due probably to auricular systole, movement of the heart during the isometric contraction period and also possibly to movement of the semilunar valve before opening[17]) are relatively insignificant, whereas the arrival of the pulse wave initiated by ejection is marked by an abrupt rise in the curve. Although these preliminary movements are rarely recognizable in roentgenkymograms of the great vessels (probably because of their small size), the beginning rise of the pulse wave is usually not so sharply defined as in the magnified curves of the optically recorded waves. In certain cases the possible error in determining the beginning of the pulse is such that the records cannot be used.

The possibility of error due to movement of the vessel as a whole was considered. This movement is doubtless a factor in all roentgenkymograms of the great vessels, particularly of the aortic knob. In certain cases with vigorous heart action, particularly those with aortic insufficiency or hyperthyroidism, the movement of the aorta at the knob may be much greater than just above the valve. We have recorded apparently distorted pulse waves here with a lateral excursion of nearly 2 cm. It seemed, however, that even at the aortic knob, movement of the vessel as a whole did not involve an appreciable error in the time relations. As a matter of fact, the error due to movement of the knob before arrival of the pulse would tend to minimize this evidence of delay in ejection from the left ventricle.

As a result of numerous measurements and controls we have concluded that with satisfactory roentgenkymograms and careful technic there remains a possible error in any individual measurement of 0.02 second. We have attempted to minimize this possible error in determining the intervals between the beginning of the QRS complex and the aortic and pulmonary artery pulse by measuring two or three intervals and taking the average (Table IV). In a few thin-chested individuals with excellent contrast, however, the film was run very rapidly and only a single pulse recorded. In these cases the speed of the film and the presence of the time signal on the film, referred to above, minimized errors in measurement.

It was hoped in the beginning of our work that cases of bundle-branch block would be encountered with either sufficient dilatation of the ascending aorta or tortuosity so that the pulses of the ascending aorta and the pulmonary artery could be recorded in the same film. No such cases were found, and it was, therefore, necessary in all cases to record the aortic pulse at the aortic knob. From available data on pulse wave velocity in large vessels and length of aorta it was estimated that the pulse at the knob should fall 0.010 to 0.015 second later than in the ascending aorta.*

*The point on the ascending aorta from which the length to the aortic knob was measured, was taken at a level comparable to that of the pulmonary artery roentgenkymogram.

TABLE IV

INTERVALS BETWEEN BEGINNING OF QRS COMPLEX AND PULSE WAVES IN AORTA AND PULMONARY ARTERY (AS MEASURED FROM ROENTGENKYMOGRAMS TIMED BY ELECTROCARDIOGRAMS)

	CASE	RATE	TO ASCENDING AORTA (SECOND)	TO AORTIC KNOB (SECOND)	TO PULMONARY ARTERY (SECOND)	INTERVAL BETWEEN PULMONIC AND AORTIC PULSE* (SECOND)	INTERVAL BETWEEN 1ST AND 2ND COMPONENT OF SPLIT FIRST SOUND
The common type of bundle-branch block	W. B.	80		0.15	0.10	+0.04	
	R. J.	92		0.15	0.10	+0.04	0.06
	M. R.	84		0.17	0.10	+0.06	
	R. B.	130		0.17	0.10	+0.06	0.06
	L. H.	80		0.22	0.14	+0.07	
	H. P.	79		0.16	0.10	+0.05	
Average		91		0.17	0.11	+0.05	
Intraventricular conduction defect and split first sound	J. O'C.†	98		0.16	0.11	+0.04	0.06
	A. O.‡	74		0.12	0.17	−0.05	0.06
Cases with normal electrocardiograms and single first sound	J. W.	75		0.14	0.11	+0.02	
	E. K.	105		0.08	0.08	−0.01	
	J. R.	158		0.08	0.04	+0.03	
	C. T.	66		0.14	0.15	−0.02	
	G. M.	100	0.12		0.12	0.00	
	D. Sh.	115	0.10		0.12	−0.02	
	D. Sm.	125		0.09	0.07	+0.01	
	W. H.	83		0.15	0.13	+0.01	
Average		103	0.11	0.11	0.10	0.00	
Cases with normal electrocardiogram and split first sound	L. P.	85		0.13	0.06	+0.06	0.06
	S. W.	100		0.12	0.17	−0.06	0.05
	N. G.	105	0.07	0.09	0.10	−0.03	0.04
	C. S.	120		0.07	0.09	−0.03	0.04
	H. B.	92	0.12		0.14	−0.02	0.04
	W. H.	94	0.11	0.12	0.14	−0.03	0.05
Average		99	0.10	0.11	0.12		

*The figures in this column give the differences in time between the arrival of the pulse in the *ascending* aorta and the pulmonary artery, as obtained from the three columns to the left. It is assumed that the pulse wave travels from the ascending aorta to the knob in 0.01 second. This correction is applied in cases of patients whose aortic pulses were photographed at the knob. The plus signs indicate that the pulmonic pulse was the first, and the minus signs that the aortic pulse was first.

†See Fig. 1 *B* for electrocardiogram.

‡See Fig. 1 *C* for electrocardiogram.

Measurements of the interval between the beginning of the QRS complex and the beginning of the pulse wave in the aorta and pulmonary artery were obtained in 6 cases with the common type of bundle-branch block and in two cases with conduction defects which did not conform to the common type of bundle-branch block (Fig. 1*B* and *C*). There are also included a series of 8 normal controls with single first sounds and 6 normal controls with split first sounds.

In the normal controls with single first sounds the intervals show considerable variation from case to case. Similar variations were observed in the intervals between the QRS complex and the beginning of the carotid pulse (Table II).* In these controls the apparent asynchronism between the aortic and pulmonic pulse was as great as 0.03 second. No significance, however, is to be ascribed to these variations, since they fall within the range of error of the method, which is not sufficiently accurate to measure such slight asynchronism.

No significant differences in the interval from the beginning of QRS complex to the beginning of the pulmonary artery pulse were found in the cases with the common type of bundle-branch block as compared with normal controls with single first heart sounds. However, in all cases of the common type of bundle-branch block, the intervals between the QRS complex and the aortic pulse showed a significant delay in ejection from the left ventricle. This is evidenced not only by comparison with the controls, but by the fact that in each case of the common type of bundle-branch block the aortic pulse fell much later than the pulmonic. It is of interest that of the two cases mentioned above with intraventricular conduction defect, one had an electrocardiogram differing markedly from the common type of bundle-branch block (Case A.O., Fig. 1*C* and Table IV), and in this case the delay in ejection was on the right side rather than on the left (Table IV).

THE RELATION BETWEEN ASYNCHRONISM IN THE BEGINNING OF EJECTION FROM THE TWO VENTRICLES AND SPLITTING OF THE FIRST HEART SOUND

The time relations of the beginning of the pulses in the aorta and pulmonary artery, as obtained by the roentgenkymographic method, offer an opportunity to test the hypothesis that splitting of the first heart sound is related to asynchronism in certain dynamic events associated with the early phases of contraction of the two ventricles (Table IV).

The time relations of the two components of a split first heart sound to the beginning of left ventricular ejection can be obtained from combined carotid artery and sound tracings recorded without parallax. An allowance of 0.02 second for transmission of the pulse from

*The data suggest that cardiac rate is one of the factors concerned in the duration of the interval; it tends to be shorter in cases with tachycardia.

the aortic valve to the carotid artery is sufficiently accurate for practical purposes. The time relations can also be easily calculated if both electrocardiogram-heart sound and electrocardiogram-carotid artery tracings, made in the same position and with similar heart rates, are available. The most satisfactory method is to record simultaneously without parallax, the electrocardiogram, sound tracing and carotid artery pulse. The only error in this method involves the assumption that the pulse requires 0.02 second to be transmitted from the aortic valve to the carotid artery.

In the measurements, we have disregarded small vibrations of an indeterminate character, probably subsonic, which frequently fall very near the beginning of the QRS complex. Large vibrations of the type which doubtless represent audible sound begin rather abruptly, usually in the range of 0.03 to 0.07 second after the beginning of the QRS complex and sometimes slightly later. That these large vibrations begin before left ventricular ejection can readily be determined by the methods mentioned above.

When the first heart sound is split, the time interval from the beginning of the QRS complex to the first component is about the same as in the case of a single first sound. If a well-damped recording apparatus is used, however, the large vibrations are found to cease abruptly, and a quiet interval is recorded until the second component of split sound occurs. The recorded vibrations of both components may be of approximately the same amplitude or they may be much larger in one component than in the other. A striking characteristic is the short duration of each sound component as compared with the prolongation that is often observed when no splitting of sound can be detected.

An attempt was made to obtain data regarding the relation between the two components of a split first sound and ventricular ejection in two cases with the common type of bundle-branch block,* two cases with other types of bundle-branch defect, and six cases with no delay of intraventricular conduction. In the four cases with conduction defect both optically recorded carotid pulse and roentgenkymographic tracings of the aortic and pulmonary artery pulses were used to determine the times of ventricular ejection. In the six cases without intraventricular conduction defect, roentgenkymographic tracings were used.

The cases with normal intraventricular conduction and split first sounds showed a significant degree of asynchronism between the beginning of right and left ventricular ejection, comparable to that of bundle-branch block and greater than that found in normal controls

*Splitting of the first sound could be detected on auscultation at times in some other cases of bundle-branch block, but because of the feebleness of the sounds could not be satisfactorily recorded. Occasionally only a single faint sound or systolic murmur could be heard and, less frequently, a faint sound and a murmur.

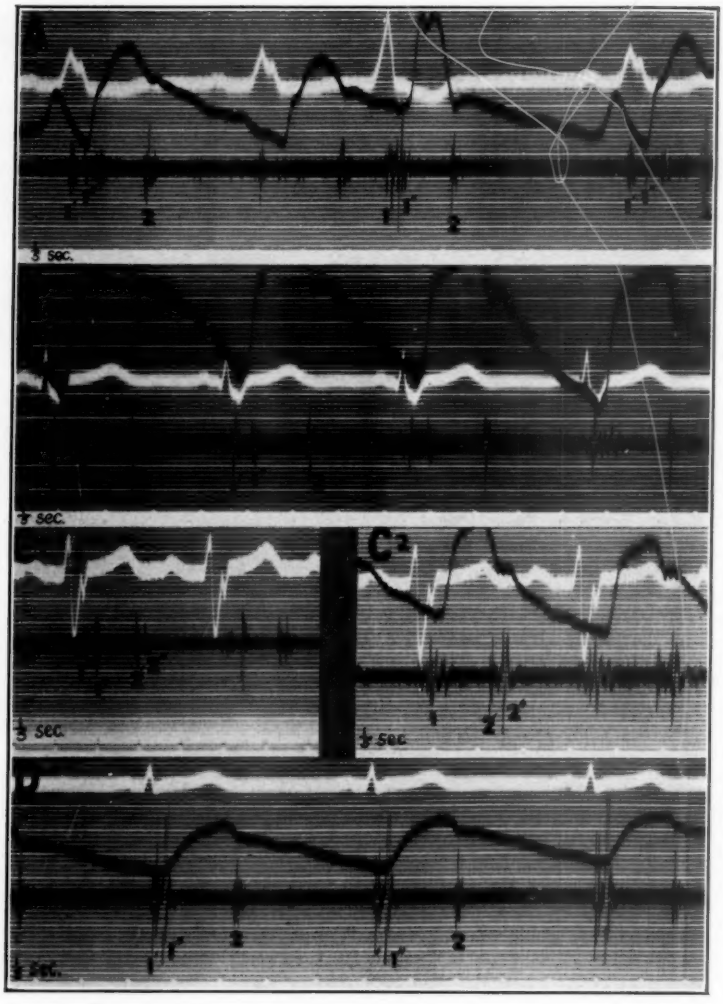

Fig. 6.—The relation of the two components of split first heart sounds to the upstroke of the carotid pulse.

***A*, Case M. R. (Table IV). The common type of bundle-branch block. The carotid upstroke follows the second component of the split first sound both in the sequential beats and in the ventricular extrasystole.**

B, Case A. O. (Table IV). The three leads of this patient's electrocardiogram are shown in Fig. 1 *C*. Intraventricular conduction defect of a type which is probably right sided. The carotid upstroke follows the first and precedes the second component of the split first sound.

C, Case J. O'C. (Table IV). The three leads of this patient's electrocardiogram are shown in Fig. 1 *B*. The tracing C_{-2} was made several months after C_{-1}. In C_{-1} the first sound is definitely split. In C_{-2} it is not split but prolonged. The upstroke of the carotid is late in relation to the beginning of the sound suggesting that the left ventricular component is the latter part of the prolonged sound.

D, Normal control with split first sound. In this case the carotid upstroke follows the second component of the split first sound. In certain normals it may follow the first and precede the second component.

(Table IV). However, in 5 of the 6 cases in this group left ventricular ejection preceded the right, and even in the case in which left ventricular ejection followed right ventricular ejection, it did not tend to be so late as in bundle-branch block.

In the two cases with the common type of bundle-branch block, the carotid pulse tracings showed clearly that ejection from the left ventricle did not begin until after completion of the second component of the split first sound (Fig. 6*A*). In one case (J. O'C, Table IV) with intraventricular conduction defect, a similar relation was observed. However, in the other case with intraventricular conduction defect of a type which we are beginning to believe is due to a lesion in the right branch,* (A.O., Table IV and Fig. 6*B*) left ventricular ejection preceded the second component of the first sound.

Because of the fact that the roentgenkymograms were made with the patient in the standing position and the sound tracings in the recumbent position, the attempt to correlate the time relations of the sounds and ejection from the two ventricles by this method is subject to possible error. In certain cases splitting of the first sound may be noted in one position or phase of respiration, and not obtained in other positions or other phases of respiration. However, in each case included in this study, the precaution was taken to determine by auscultation that, with the patient in the standing position and holding his breath, splitting of the first sound was present just before and after the roentgenkymograms were made.

The data, as obtained by roentgenkymography, regarding relationships of ventricular ejection from the two ventricles to the two components of split first sounds are presented in Table IV. The relations observed are as follows: (1) Although significant asynchronism in ejection may occur without demonstrable splitting of heart sounds (possibly because of feebleness or inaudibility of one component), it was present in all cases studied with widely split first sounds. (2) The first component of the split first sound invariably precedes ejection from either ventricle. (3) If the split between the two components of sound is wide, ejection from one ventricle (in some cases the right, in others the left) may precede the second component of sound, or the two may be practically synchronous. (4) The second sound component invariably precedes ejection from the later ventricle. (5) The first component of sound precedes ejection from one ventricle by approximately the same interval that the second component precedes ejection from the other ventricle.

Asynchronism in the onset of ejection might be due to (1) asynchronism in the onset of contraction in the two ventricles, (2) differ-

*F. N. Wilson and his coworkers[26] have presented evidence, derived from electrocardiograms that record the potential variations produced by the heartbeat at a single point, which supports this view.

ences in duration of the isometric contraction phase in the two ventricles. Both mechanisms may be operative in the same case and may either increase or diminish the degree of asynchronism. Presumably in cases of bundle-branch block asynchronism depends mainly on delay in the onset of contraction in one ventricle, due to delay in the arrival of the excitatory process. However, it does not seem reasonable to suppose that a similar delay may occur when intraventricular conduction is normal. Under such circumstances differences in the isometric contraction phase may occur, possibly due to different dynamic factors in the two ventricles. Failure to consider this possibility has led many observers to the conclusion that asynchronism in contraction is impossible when the electrocardiogram is normal.

According to Wiggers and Dean,[27] the main vibrations of the first heart sound coincide with the beginning of the intraventricular pressure rise. While it is certain that the first heart sound is initiated during the isometric contraction phase, and that it is probably due to rapid rise of intraventricular tension, we are not concerned with the actual mechanism of sound production at present. We do wish, however, to emphasize the fact that, when the first sound is split, each component begins before the end of the isometric contraction phase of one ventricle or the other. The asynchronism in sound as well as the onset of ejection is therefore related to asynchronism of some event during the isometric period.

The foregoing observations have certain applications to the consideration of single first heart sounds. It would appear that the important duality is composed of the right and left ventricular components of sound. So-called prolonged or impure first sounds are sometimes, possibly always, due to imperfect synchronism of the right and left ventricular sound components. That this is the case can actually be demonstrated in some cases with phasic splitting of the first sound, in which at some times prolonged first sounds and at other times split sounds may be recorded. Therefore the view not infrequently expressed that prolonged or impure first sounds are to be regarded as evidence of cardiac muscle abnormality should be reconsidered.

Possibly one of the reasons why investigators have made so little progress in determining the mechanism of production of the first heart sound has been failure to take into account the right and left ventricular contributions to the sound. This problem can be simplified, to some extent at least, if the sound production of one ventricle is studied separately from that of the other ventricle. As a matter of fact such a separation is essential if accuracy is to be obtained in recording time relations.

THE RELATION BETWEEN ASYNCHRONISM IN THE END OF EJECTION FROM THE TWO VENTRICLES AND SPLITTING OF THE SECOND SOUND

The end of the ejection phase is marked by the sounds due to closure of the semilunar valves, although as pointed out by Wiggers, actual ejection ceases shortly before valve closure.[17] However, practical

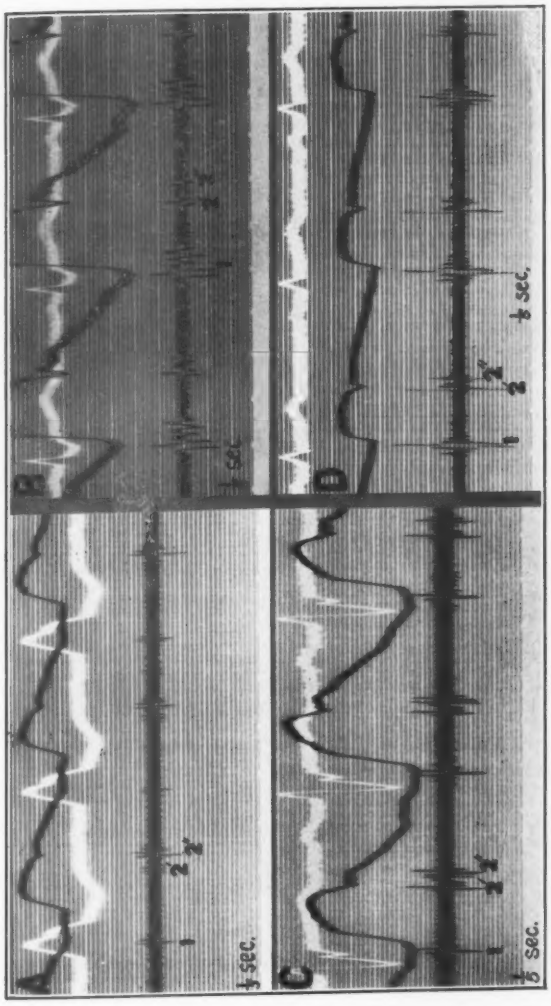

Fig. 7.—The relation of the carotid incisura to split second sounds.

A, Same case as shown in Fig. 6 *A*. The common type of bundle-branch block. The carotid incisura follows the second component of the split second sound.

B, Same case as shown in Fig. 6 *B*. Probable right-sided intraventricular conduction defect. The carotid incisura follows the first and precedes the second component of the split second sound.

C, Same case as shown in Fig. 6 *C*. Intraventricular conduction defect, side of lesion questionable. The carotid incisura follows the first and precedes the second component of the split sound. All the data in this case indicate that pulmonic ejection begins ahead of aortic ejection and ends later.

D, Normal control. The carotid incisura follows the first and precedes the second component of the split second sound. In certain normal controls the carotid incisura may follow the second component.

difficulty is often encountered in the attempt to measure the end of ejection by the second sound, since the sound is frequently split both in normal and in diseased hearts. In bundle-branch block there tends to be unusually wide splitting of the second sound.* In normals, the

*Rarely the second sound in bundle-branch block shows merging of the two components or only slight splitting. In one case in which the latter occurred, the ejection period in the left ventricle, as calculated from the carotid pulse, was unusually short (0.21 sec., Case E. G. Table II).

second sound may be (1) single, (2) split in every beat, or there may be (3) respiratory phasic incidence of splitting.[28] Phasic incidence of splitting was not observed in our cases of bundle-branch block.

In view of these facts it seemed advisable to test the hypothesis that splitting of the second sound is due to asynchronism in closure of the aortic and pulmonic valves.

Whenever the second sound is definitely split, the component identified with aortic closure can be determined readily by comparing the time relations of the second sound to the incisura (dicrotic notch) of the optically recorded carotid pulse. Since the wave forming the ascending limb of the incisura is reflected as a result of aortic closure, it should reach the carotid artery approximately 0.015 to 0.025 second after aortic closure. Consequently the sound due to aortic closure should precede the bottom of the carotid incisura by approximately this same interval.

TABLE V

TIME INTERVALS IN CASES OF THE COMMON TYPE OF BUNDLE-BRANCH BLOCK BETWEEN EACH COMPONENT OF THE SPLIT SECOND SOUND AND THE INCISURA OF THE RIGHT CAROTID ARTERY PULSE			TIME INTERVALS IN THE COMMON TYPE OF BUNDLE-BRANCH BLOCK BETWEEN EACH COMPONENT OF THE SPLIT SECOND SOUND AND THE BEGINNING OF THE DESCENDING LIMB OF THE JUGULAR V-WAVE		
CASE	1ST COMPONENT (SECOND)	2ND COMPONENT* (SECOND)	CASE	1ST COMPONENT† (SECOND)	2ND COMPONENT (SECOND)
H. P.	0.07	0.02	H. P.	0.08	0.04
R. J.	0.10	0.01	M. R.	0.08	0.02
M. R.	0.06	0.01	L. H.	0.11	0.04
L. H.	0.07	0.01	R. B.	0.12	0.06
R. B.	0.07	0.02	W. W.	0.08	0.03
E. G.	0.08	0.02			
H. H.	0.04 to 0.06	0.01 to 0.02			

*The time relations of the second component indicate that it represents aortic closure in all cases studied.

†The interval between pulmonic closure and the beginning descent of the V-wave measures approximately the duration of the isometric relaxation phase of the right ventricle. The normal range is 0.06 to 0.13 second. Therefore, in Cases H. P., M. R., L. H. and W. W., the first component must represent pulmonic closure. In Case R. B. the second component was found by its relation to the carotid incisura to represent aortic closure. Thus it would appear that in this case also the first component represents pulmonic closure.

Observations were made in 7 cases with the common type of bundle-branch block possessing split second sounds (Table V and Fig. 7*A*). In all of the 7 cases, the incisura bore a significant time relation to the second component of the split second sound and never to the first component. Similar studies have been made in other types of cases having split second sounds (with and without intraventricular conduction defect, Fig. 7 *B*, *C* and *D*). In these cases, in contrast with the findings in the common type of bundle-branch block, aortic closure is frequently identified with the first component of the split sound.

The method used for attempting to identify pulmonic closure depends on the duration of the isometric relaxation phase as measured

from the second heart sound to the beginning of descent of the V-wave in the optically recorded pulse from the veins just above the right clavicle. Wiggers[17] states that the isometric relaxation phase can be determined by measuring the interval between the bottom of the incisura of arterial pulse and the beginning of the V-wave drop in the venous pulse in the neck. Since the first depends on left ventricular and the second on right ventricular action the interval between them

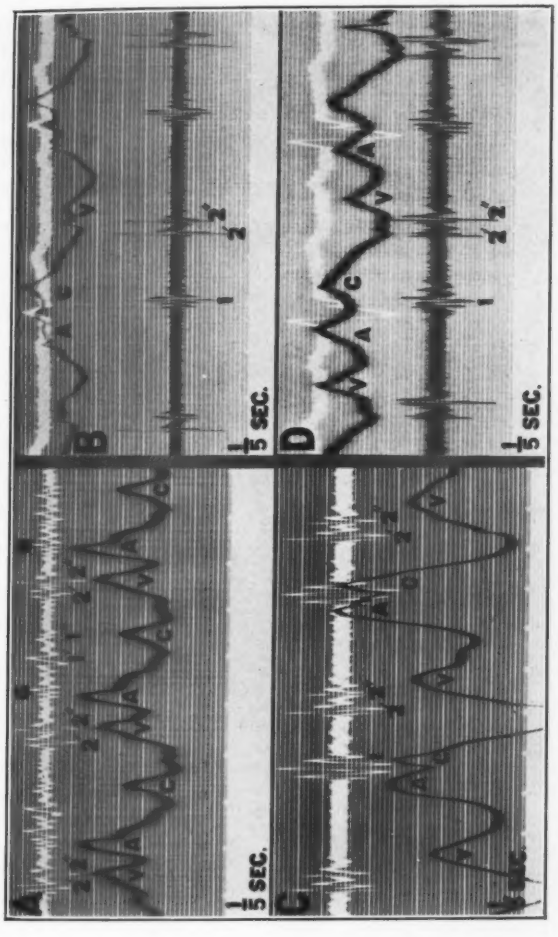

Fig. 8.—The relation of the V-wave of the jugular pulse to the components of split second sounds. The duration of the isometric relaxation phase is in the range of 0.06 to 0.13 second at ordinary heart rates. Thus pulmonic closure should precede the beginning descent of the V-wave in the same range.

A, The common type of bundle-branch block. The beginning descent of the V-wave bears a significant relation to the first (and not to the second) component of the split second sound.

B, Normal control. Same case as shown in Fig. 7 *D*. The descent of the V-wave falls 0.11 second after the first and 0.06 second after the second component of the split second sound. Therefore, the method is of no value in this case in determining pulmonic closure. The time relations to the carotid incisura indicated that the first component was aortic. Presumably, therefore, the second component is pulmonic.

C, Same case as shown in Fig. 7 *B*. 8 *D* is same case as in Fig. 7 *C*. In both cases the descent of the V-wave bears a significant relation to the second component of the split second sound and not to the first component. The second component in both cases, therefore, must represent pulmonic closure. In Fig. 7 it was shown in both cases that the relation of the second sounds to the carotid incisura indicated that the first component represented aortic closure.

may be regarded as an index of the isometric relaxation phase *only* when aortic and pulmonic closure are synchronous. Since Katz[15] has shown that these events are usually asynchronous in dogs, and the frequency of split second sounds suggests that they are often asynchronous in human beings, the accuracy of the method used by Wiggers is not established except for cases with single second sounds.

In a previous report[25] we presented data on the duration of the isometric relaxation phase as measured from the second heart sound

(1) to the beginning descent of the V-wave and (2) to the opening snap in mitral stenosis. It was found that cardiac rate is a factor in the duration of the isometric relaxation phase. At ordinary heart rates, the duration of this phase tended to fall in the range of 0.07 to 0.12 second with outside limits of 0.06 to 0.13 second. In the presence of extreme tachycardia, the interval may be as short as 0.04 second and in marked bradycardia as long as 0.19 second. Another fact which emerged from that study was that when the second heart sound is single, in cases of mitral stenosis with the opening snap, the beginning descent of the V-wave (which marks the end of the isometric relaxation phase of the right ventricle) tends to fall at the same instant as the snap (which marks the end of the isometric relaxation phase in the left ventricle). However, when the second sound is definitely split, the descent of the V-wave begins either before or after

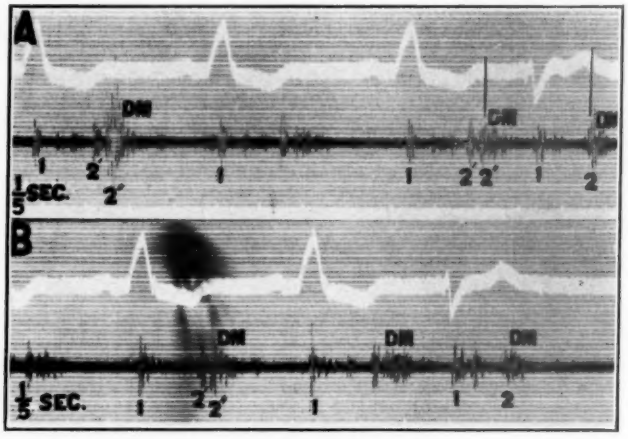

Fig. 9.—Case R. J. (Tables II and IV, also Fig. 3 *C*). The relationship of the diastolic murmur of aortic regurgitation to the second heart sound in the common type of bundle-branch block. The murmur is continuous with the second component except in extrasystoles with the main QRS complex oppositely directed to the rhythmic beats. In the extrasystoles the murmur is continuous with the beginning of the second sound. The time of the carotid incisura (obtained from Fig. 3 *C*) is shown on the last two beats of the top strip. This point should follow the beginning of aortic regurgitation by approximately 0.02 second.

the opening snap, indicating that under these circumstances, the isometric relaxation period does not tend to end synchronously in the two ventricles.

The time relations of the V-wave in the optically recorded pulse of the veins just above the clavicle were compared with the two components of the split second sound in the common type of bundle-branch block in 5 cases (Table V). In each case, the interval between the first component of the split second sound and the descent of the V-wave falls within the customary range found when the second sound is single. In 4 of the 5 cases the interval from the second component of the second sound was shorter than that of isometric relaxation

phases recorded at comparable heart rates (Fig. 8), and in the fifth case (R. B.) both components of the second sound fell within the significant range (0.06 and 0.12 second).

From these data the following may be said regarding the common type of bundle-branch block: when splitting of the second sound is recorded, the first component is due to pulmonic closure and the second component to aortic closure. Therefore, ejection from the right ventricle ends earlier than that from the left ventricle. According to the intervals recorded between the two components of the second sound

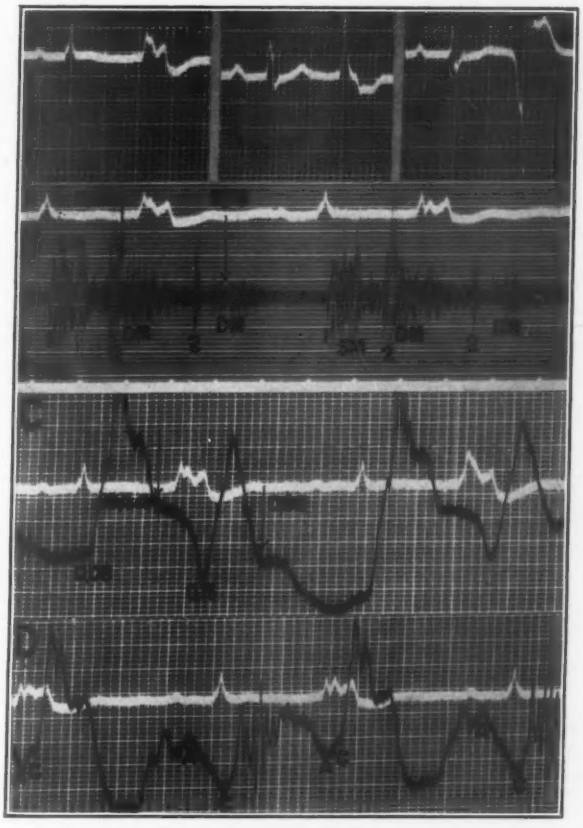

Fig. 10.—A patient with aortic regurgitation and ventricular extrasystoles with main QRS deflections upward in Lead I and downward in Lead III.

A, Electrocardiographic Leads I, II and III.

B, Lead I and sound tracing. In the normal beats no gap is recorded between the second sound (2) and the diastolic murmur (DM), but in the extrasystolic beats a wide gap is present (0.08 second).

C, Lead I and carotid artery tracing. The interval between the beginning of the QRS complex and the upstroke of the carotid is 0.08 second in normal beats and 0.16 second in extrasystolic beats. There is no definite incisura due to the free aortic regurgitation, its position being marked by sudden angulation in the wave (arrows). This point which should follow the beginning of aortic regurgitation by approximately 0.02 second has been marked off (arrows) on the sound tracing in *B*.

D, Lead I and jugular pulse tracing. There is apparently no delay in the venous C-wave in extrasystolic beats comparable to that of the carotid wave. The actual measurement is somewhat obscured by the presence of an A-wave.

in our cases, ejection ended on the right side from 0.03 to 0.09 second before it ended on the left. The conclusion that in the common type of bundle-branch block, aortic closure tends to follow pulmonic closure may be further tested by studying cases with valvular lesions which produce murmurs or sounds having a definite relationship to aortic closure.

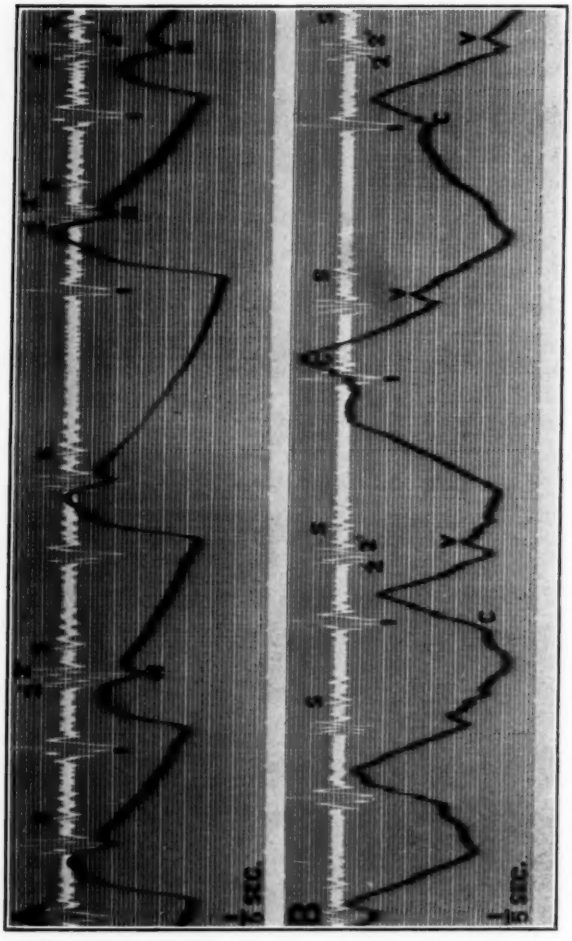

Fig. 11.—Case H. H. (Table II and Fig. 2 *C* and Fig. 3 *A*). Exhibiting the common type of bundle-branch block, auricular fibrillation, a split second sound, and the opening snap of mitral stenosis.

A, Sound (recorded by the electrocardiographic string) and carotid artery tracing. The carotid incisura (n) identifies the second component of the second sound as being due to aortic closure. The time relations of the opening snap (s) to the two components also indicate that the second component must be aortic closure (time to opening snap 0.10 second), since the interval between the first component and the snap is too long for a significant relationship (0.16 second).

B, Sound and jugular pulse tracing. The time relations of the beginning descent of the V-wave to the second sound (0.11 second between first component and V-wave drop) indicate that the first component must be pulmonic closure. Thus three separate procedures for identifying components of split second sounds (time relations to carotid incisura, descent of V-wave, and the opening snap) give concordant results. Furthermore, the beginning descent of the V-wave (which marks the end of the isometric relaxation phase in the right ventricle) precedes the opening snap (which marks the end of the isometric relaxation phase in the left ventricle) by approximately 0.06 second. The asynchronism in this case is due mainly to the fact that the isometric relaxation phase begins earlier in the right ventricle and ends earlier, rather than to unequal duration in the two ventricles.

We have had the opportunity to make fairly complete studies in one case with the common type of bundle-branch block and well-developed aortic insufficiency (Case R. J., Tables II and IV). It is well known that the murmur of aortic insufficiency is either practically continuous with or replaces the aortic second sound. It was noted in this case, both by auscultation and by sound tracings (Fig. 9), that the diastolic murmur was continuous with the second component of the split second sound. However, when ventricular extrasystoles with

the main QRS deflection downward in Lead I occurred, the murmur was continuous with the first component. These findings indicate that in the beats exhibiting the common type of bundle-branch block, the second component of the split second sound was identified with aortic closure.

Studies of a similar nature were made in a patient exhibiting aortic insufficiency, intraventricular conduction time within normal limits in sequential beats, and occasional ventricular extrasystoles with QRS complexes, upward in Lead I, and downward in Lead III, somewhat resembling although not identical with those found in the common type of bundle-branch block (Fig. 10*A*). It was found in the sequential beats that the carotid pulse and the C-wave obtained over the right jugular vein began 0.08 second after the initial wave of the QRS complex (Fig. 10 *C* and *D*). Sound tracings showed that the diastolic murmur due to aortic insufficiency was practically continuous with the second heart sound in the sequential beats (Fig. 10*B*). In the extrasystolic beats, however, the carotid pulse was delayed, beginning 0.16 second after the initial wave of the QRS complex (Fig. 10*C*), although the venous C-wave maintained the same time relations of 0.08 second to the QRS complex as it did in sequential beats (Fig. 10*D*). Furthermore, in the premature beats the diastolic murmur did not follow immediately after the second sound but there was a gap between them of 0.09 second. It would therefore appear that in these extrasystolic beats the delay was limited to the left side and that the extrasystoles must have originated in the right ventricle.

In mitral stenosis the opening snap is associated with the attempt of the crippled mitral valve to open.[25] It is therefore closely related in time to the end of the isometric relaxation phase of the left ventricle. It bears a definite time relation, in any given case, to aortic closure, being uninfluenced by relative shifts in the position of pulmonic closure. Thus, the component of a split second sound which represents aortic closure can be identified in certain cases of mitral stenosis by this time relation, as well as by the incisura of the carotid pulse. In our one case of mitral stenosis with the common type of bundle-branch block, both methods showed that the second component of the split second sound was aortic (Fig. 11). In one case with ventricular extrasystoles having complexes homologous to those of the common type of bundle-branch block, aortic closure in the extrasystolic beats was represented by the second component of the split second sound.[25*] In another case with extrasystoles of the opposite type, aortic closure in the extrasystolic beats was represented by the first component of the split second sound.[25†]

*Fig. 6, Strip I-A in reference 25.
†Fig. 6, Strip 3 in reference 25.

In control cases with widely split second sounds, whether or not intraventricular conduction defect be present, the time relations between the two components of the second sound and the beginning descent of the V-wave show that in some of these cases, in contrast to the findings in the common type of bundle-branch block, the second component represents pulmonic closure (Fig. 8*B*).

SUMMARY

Graphic studies of comparable time relations of certain events associated with the heartbeat in the common type of bundle-branch block and various types of control cases reveal the following:

1. A systolic bifid apex impulse can be recorded in some, but not in all, cases of bundle-branch block. It may also occur in cases without bundle-branch block. These facts should be considered in assessing the diagnostic value of the systolic bifid apex impulse and indicate that it cannot be regarded as reliable evidence of the presence of bundle-branch block.

2. Comparison of the interval between the beginning of the QRS complex and the beginning of the carotid pulse wave in cases with bundle-branch block, in normal controls, and in cases with cardiac decompensation, indicates that ejection from the left ventricle is significantly delayed in the common type of bundle-branch block. No comparable delay is observed in cases of cardiac decompensation without intraventricular conduction defect. Evidence is presented to establish the fact that the delay is associated with the particular type of aberrant spread of the excitatory process which occurs in the common type of bundle-branch block.

3. Comparison of the intervals between the beginning of the QRS complex and the beginning of the C-wave recorded from the veins immediately above the right clavicle in cases of the common type of bundle-branch block and normal controls shows no significant delay in bundle-branch block. This finding suggests, although it does not definitely prove, that in the common type of bundle-branch block there is no significant delay in the contraction of the right ventricle.

4. Roentgenkymographic tracings of the aorta and pulmonary artery were made in 6 cases with the common type of bundle-branch block, 2 cases with other types of intraventricular conduction defect and split first sounds, 8 normal controls with single first sounds, and 6 cases with split first heart sound, but without intraventricular conduction defect. The time relations of the aortic and pulmonary artery pulses were compared. The results were as follows: (a) In the common type of bundle-branch block, the interval between the beginning of the QRS complex and the beginning of the aortic pulse was significantly prolonged in each case. (b) In the normal controls with

single first sounds the differences in time between the beginning of the aortic and pulmonary artery pulses fell within the limits of error of the method. (c) In the cases with split first sounds, both with and without intraventricular conduction defects, the differences in time between the beginning of the aortic and pulmonary artery pulses tended to be greater than in the control cases with single first sounds. In 2 cases the differences were as great as those observed in bundle-branch block. However, in one of these two cases the aortic pulse preceded the pulmonic; whereas in all cases of the common type of bundle-branch block, the pulmonary artery pulse preceded the aortic.

5. All the findings support the hypothesis that in the common type of bundle-branch block there is asynchronism in the beginning of ejection from the two ventricles due to delay on the left side. The evidence also indicates that in some, possibly all, cases with split first sounds but without intraventricular conduction defect, there is asynchronism in the beginning of ejection from the two ventricles.

6. The association between asynchronism in the beginning of ejection from the two ventricles and splitting of the first heart sound; the correspondence in the intervals between the two components of the sounds and the degree of asynchronism; and the relationship of the arterial pulse to one or the other component indicate that (1) the split first sound has a right ventricular and a left ventricular component, and that (2) separation of these components is due to asynchronism in certain of the early phases of cardiac contraction in the two ventricles.

7. Splitting of the second heart sound can be heard on auscultation and recorded in most cases with bundle-branch block. It is also frequently present in cases without evidence of cardiovascular damage.

8. It can be proved by the following methods for identifying aortic and pulmonic closure that splitting of the second heart sounds is due to asynchronism in closure of the two semilunar valves. (a) When the second heart sound is split, the component associated with aortic closure can be identified by its time relation to the incisura of the carotid artery pulse. (b) When the sound is *widely* split, the component associated with pulmonic closure can be identified by its time relations to the beginning of the descent of the V-wave recorded from the veins above the clavicle. (c) When either the diastolic murmur of aortic insufficiency or the opening snap of mitral stenosis is present, additional methods for confirming the identity of the components of the second sound may be available.

9. In the common type of bundle-branch block, pulmonic closure usually precedes aortic closure. Occasionally they may be practically synchronous.

10. In cases with split second sounds but without intraventricular conduction defect, either aortic or pulmonic closure may come first.

11. All the evidence obtained in this study is in accord with the hypothesis that the common type of bundle-branch block is due to delay in spread of the impulse on the left side. The view held by Eppinger and Rothberger, and Lewis is no longer tenable. No support was obtained for the statement that it is unjustifiable to attempt to localize the side of bundle-branch block from the direction of the major initial complex in the three limb leads of the electrocardiogram.

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A NEW METHOD FOR THE RECORDING OF HEART SOUNDS*

MYRON M. SCHWARZSCHILD, M.A., AND MILTON D. FELTENSTEIN, M.D.
NEW YORK, N. Y.

SINCE heart-sound registration has thus far failed to correspond with auscultatory findings, most clinicians have taken little interest in these investigations. Clinical cardiology is based primarily upon the response of the human ear, and the various methods of recording heart sounds do not correspond to the obvious auditory impression. Thus, one often reads reports of heart-sound registration in which the author states that a particular recorded sound is inaudible. The purpose of this study has been to introduce distortion so as to duplicate mechanically the failings of the human ear. Another difficulty in reading the graphs so far reported, resides in the impossibility of determining when a sound begins or ends, for the base line merges into the sound, which presents no sharp and easily recognizable distinction. Such records, therefore, do not fulfill their primary purpose, which is the exact timing of the heart.

It would be possible to construct a system of cardiology based upon the findings of the type of mechanical registration which we have just discussed. Such a system, however, would bear no relation to clinical cardiology as it is practiced today. We trust that the following report will show that heart-sound registration can be made to correlate with clinical findings, and can be employed readily and with as much ease as electrocardiographic study for the elucidation of cardiac pathology.

THEORETICAL

There are numerous methods available for the recording of sound in general and of heart sounds in particular. The features common to all such methods are (1) a receiver for the sound and (2) a recorder which registers, usually by optical methods, the motion of some part of the recording apparatus. These devices have been constructed so as to make the motion of the recorder or, more strictly, the recording light-beam an exact reproduction, on an enlarged scale, of the motion of the diaphragm or other suitable part of the receiver. It was found early in the history of heart-sound registration that many murmurs could be recorded more clearly if distortion were introduced into the system in such a direction as to stress higher frequencies. The scale of enlargement was made to vary with the frequency of the sound in such a way that higher frequencies were enlarged to a greater extent

*From the departments of Physics and Medicine, Beth Israel Hospital.

than lower frequencies. Distortion is also found to be necessary if the apical impulse, which is a strong mechanical vibration, but entirely inaudible, is not to appear in the record.

Detailed analysis of the many previous methods of introducing distortion is unnecessary. Suffice it to indicate that they were usually of a haphazard nature, sometimes consisting of the introduction of a sidearm opening in a recording capsule, at other times of the use of a transformer or condenser in an electrical recording system. But, to our knowledge, there has never been any quantitative requirement set on this distortion.

It is the aim of this work to set up definite requirements for this frequency distortion. We require that the sound record be one readily

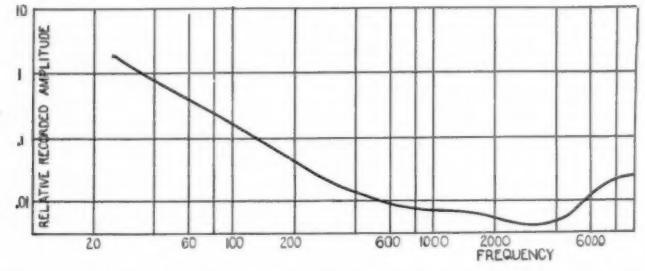

Fig. 1.—The amplitude recorded by a sound pressure recorder of uniform frequency response to sounds of various frequency of the same loudness level (30 D B., A.I.E.E. Standard) Electrical Engineering, November, 1933, 52-11-p. 745.

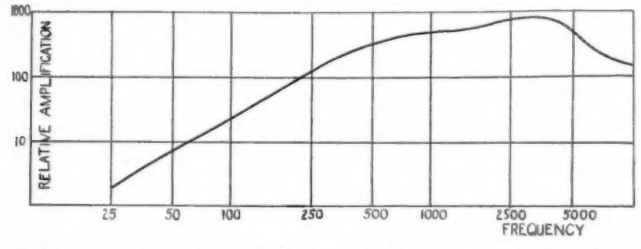

Fig. 2.—Relative amplification required at various frequencies so that sound pressure records yield equal amplitudes for equal loudness level (30 D B) at all frequencies.

interpretable in terms of the sounds heard by the ear, in order that the mass of clinical experience in auscultation may be applied without difficulty to a heart-sound record. Our criteria must depend upon the typical response of a normal ear. Fig. 1 shows the amplitude of deflection which would be registered by a distortionless sound pressure recorder responding to pure notes of low intensity and of the same loudness, as judged by the average ear. It is evident that our requirement may now be put into exact quantitative terms. Distortion must be so introduced that the amplitudes of deflection for various frequencies are equal for the same loudness. The distortion must therefore be of the type shown in Fig. 2. There should be no recorded

amplitude for vibrations of any magnitude of frequency outside audible limits and the magnifications must increase strongly with increased frequency up to about 3000 cycles, and then decrease to the upper limit of audibility. As a practical matter we may neglect all frequencies above 1000. First, there are practically no important heart sounds of dominant frequencies above this point; and second, the speed of the film necessary to record higher frequencies would produce a record of unwieldy length.

We have constructed a recorder in fair approximation to these principles. It consists of (1) an electromagnetic receiver which is strapped to the patient, (2) a high gain amplifier in which, by appropriate choice of circuit constants, the necessary distortion is introduced, and (3) an electromagnetic oscillograph throwing a moving light-beam into the camera slit of an electrocardiograph, also connected to the patient. Because of difficulties which we hope to remove in the future it has been impossible to introduce quite as much distortion as is theoretically required, but our existing apparatus represents a reasonable approach to the ideal.

In viewing the records, another factor of great importance must be considered. The ear, like other sense organs, is characterized by a logarithmic response. That is to say, sounds differing by equal sensation differences, possess amplitudes differing not by a constant amount but by a constant factor. For example, if four sounds differ by equal sensation level differences and the recorded amplitudes of the first and second are respectively one and two millimeters, then the third and fourth will be represented by amplitudes of four and eight millimeters respectively. Consequently, records represent relative loudness of different sounds only in a very qualitative way. These deviations from what might be termed a true auditory record are inherent in all the methods of recording and cannot be obviated by any pure frequency distortion. There is, however, a way of overcoming these difficulties by means of a method which we expect to report in the future.

In spite of all the deviations of the present system from the ideal, the improvement upon all other methods is marked. We do not record the inaudible low frequency vibrations so evident in the records of other experimenters. We have had no case of recorded sounds which on careful auscultation could not be heard, and we have recorded all audible sounds. Our records have this in common with any system, that they enable much more accurate conclusions, based on timing, to be drawn than the unaided sense organs permit.

PROCEDURE

This method of heart sound registration is extremely simple. All that is required is a stationary set-up which is more or less perma-

nently adjusted, and a quiet room. The microphone is strapped to the patient's chest. He is instructed to hold his breath during the recording, which takes fifteen to thirty seconds. The entire procedure consumes no more than five minutes and is performed with no discomfort to the patient. The apparatus is not fragile and easily permits one to take eight or nine records in an hour.

Base Line.—The ideal base line would be a solid streak without vibrations which would facilitate enormously the legibility of sound registration. Apparently, this is extremely difficult to obtain in an electrical circuit with the high amplification required. It will be noted that our records show a base line consisting of a uniform frequency and amplitude. With practice in reading, one is soon able to observe the slightest irregularity in this line. Hence, the beginning of the heart sounds can be timed with precision. The instant of change from

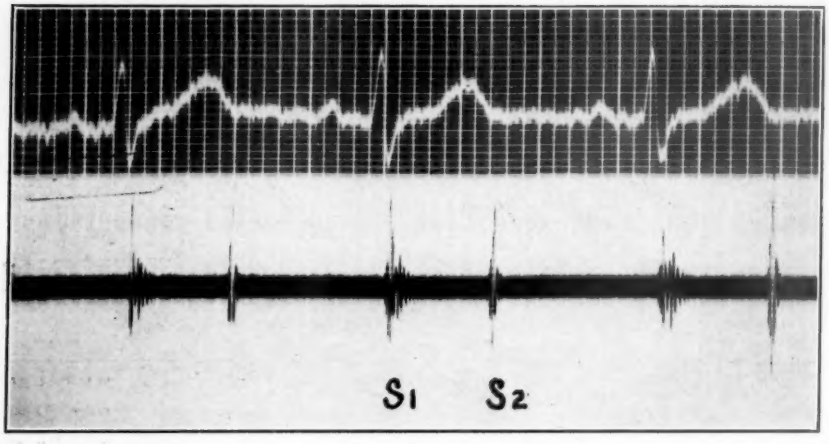

Fig. 3.—Male, twenty-six years old, normal heart. Sounds at apex. Serrated first sound and second sound. No murmurs. Record S_1 begins on terminal portion of down stroke of R-wave, duration 4/50 sec. Begins with two low amplitude vibrations, followed by higher amplitude, higher frequency element, ends with gradual decrescendo of lower frequency.

S_2 begins at end of down stroke of T-wave, duration 2/50 sec. Begins with moderate amplitude and high frequency, followed by higher amplitude and higher frequency element, ends with fast decrescendo of lower frequency.

S_1, first sound at apex; S_2, second sound at apex.

NOTE: The "serrated" first sound is caused by the marked changes in frequency.

the base line is independent of the recording amplification used, although naturally the larger the amplification the more obvious the change.

Artefacts.—Numerous artefacts will appear in records. They are determinable largely by their irregular distribution and lack of rhythm. They are produced in the following ways: (1) breathing of the patient (the patient is cautioned to hold his breath while the film is running); (2) tension of the chest and muscles (if the patient does not hold his body in relaxation, irregular sounds are produced); (3) extraneous sounds (the extreme sensitivity of the mechanism re-

sponds to all sorts of noises in the environment such as vibration of the building, distant noise, borborygmus, etc.).

CHARACTERISTICS OF THE FIRST AND SECOND HEART SOUNDS

Time.—In these records the first heart sound begins simultaneously with the down stroke of the R-wave of the electrocardiogram. It never begins sooner than the apex of the R-wave.* Hence, any sound registered before the apex of the R-wave would be diastolic in time. The second sound occurs simultaneously with the second half of the down stroke of the T-wave.

Duration.—In our series, the first sound varies between 0.04 and 0.12 second. Any sound longer than 0.12 second includes a murmur. The second sound lasts 0.04 to 0.06 second.

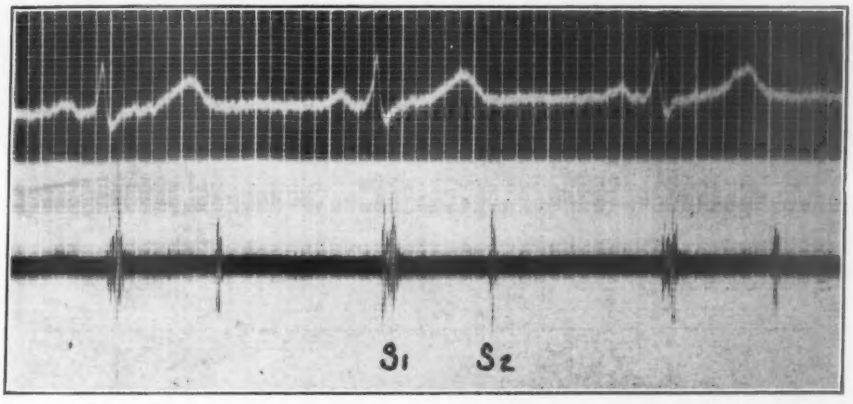

Fig. 4.—Male, thirteen years old. Catarrhal Jaundice. Normal Heart. At apex are heard a split first sound and a second sound. No murmurs.

Record S_1 begins at lower third of down stroke of R-wave, duration 4/50 sec. S_1 begins abruptly with high amplitude and high frequency, is definitely split, the second part of the split sound being of higher amplitude, ends with a decrescendo of lower frequency and amplitude.

S_2 begins at the end of the down stroke of the T-wave, duration 2/50 sec. Begins abruptly with high frequency and high amplitude, ends with a slight decrescendo.

S_1, first sound at apex; S_2 second sound at apex.

Frequency.—The frequencies of the sounds are mixed. By means of a measuring microscope we have been able to determine the frequency of each oscillation of the graph. We find a large range of frequencies, and are reporting only the dominant ranges in this paper. The dominant frequencies range between 50 and 300 cycles a second. The first sound generally shows one to three low amplitude, low frequency vibrations (about 50 per second), followed by a higher amplitude, higher frequency component (100 to 300), which is in turn followed by a decrescendo usually of lower frequency than the major com-

*We have no explanation for the apparent significance of the apex of the R-wave; however we have found no exception to this rule even in cases of widened QRS complexes.

ponent. This last corresponds with the auscultatory finding, for generally the first heart sound has a clearly decrescendo ending. The second heart sound generally starts abruptly with high amplitude and without preliminary low amplitude components. Most frequently it ends abruptly as it has begun, though occasionally there is a decrescendo finish.

Figs 3, 4, and 5 illustrate the various points.

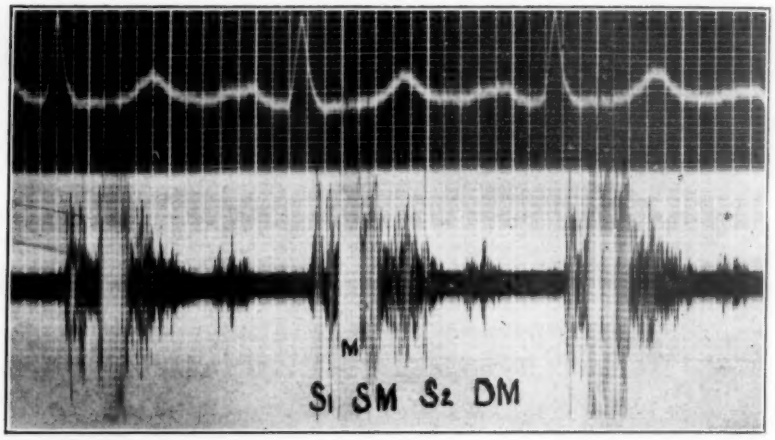

Fig. 5.—Male, thirteen years old, with active rheumatic fever. Over apex is heard a long systolic murmur in which the first sound cannot be distinguished. Part of systole is occupied by a loud musical murmur. The systolic murmur is continuous with the second sound, and after a short diastolic interval a diastolic murmur is heard. There is no presystolic element to the diastolic murmur.

Record S_1 begins on the down stroke of the R-wave, and is continuous with a long systolic murmur occupying all of systole. This in turn is continuous with the second sound. Then there is a noiseless interval for 2/50 sec. followed by a diastolic murmur lasting 5/50 sec. Presystole is free of sound.

NOTE: A musical murmur of very high frequency and amplitude occupies part of systole.

S_1, first sound at apex; SM, systolic murmur; M, musical murmur; S_2, second sound at apex; DM, diastolic murmur.

SUMMARY

We have presented a new type of recording apparatus which possesses distortion simulating that of the human ear. This permits strict correlation between clinical cardiology and phonocardiographic records. In addition we have established an even base line which permits accurate timing of the beginning and end of heart sounds. The fundamental characteristics of the first and second sounds are described.

We suggest that further phonocardiographic studies be performed along these lines. This may be expected to yield more fruitful results than has hitherto been possible.*

Our thanks are due to Dr. Marcus A. Rothschild, without whose enthusiasm and assistance this study could not have been undertaken.

*Since offering this paper for publication, our attention has been called to the work of Posener and Trendelenburg (Ztschr. f. Kreislaufforsch. 21: 15, 1929) who employed a principle quite similar to that offered here. To our knowledge they have not described their technic in detail.

THE COURSE OF RHEUMATIC HEART DISEASE IN ADULTS*†‡

I. Factors Pertaining to Age at Initial Infection, the Development of Cardiac Insufficiency, Duration of Life and Cause of Death

Arthur C. DeGraff, M.D., and Claire Lingg, M.A.
New York, N. Y.

INTRODUCTION BY ALFRED E. COHN, M.D., NEW YORK, N. Y.

A FOREWORD to these reports of Dr. DeGraff and Miss Lingg would scarcely be necessary were it not that consciously in their investigation a method of analysis was utilized, the power of which for their purpose is sometimes not fully realized. Though a foreword is perhaps unnecessary, there are implications in their study to which attention may, nevertheless, be profitably directed. A method is wanted in analyzing events in the course of long-drawn-out diseases which is not essential in studying the brief illnesses of infectious origin, to which attention has been so predominantly directed these two or three generations past. The association of lesion with structural defect, of form with function, is readily established in diseases of brief duration. The changes in the lungs in the course of lobar pneumonia, at least in their superficial aspects, are well known, though many problems no doubt remain to be solved. These diseases are attended furthermore by so many unequivocal signs and symptoms as to render relatively simple and transparent their dependence on the temporary alterations in structure which underlie them. How to arrive at an understanding of average behavior is, moreover, more or less appreciated by those who have concerned themselves with the effort to estimate the significance of these correlations and have attempted to weigh the influence of therapeutic agents on the course of these diseases. All this is, relatively speaking, simple; what are generally regarded as phenomena relevant to an illness occur so quickly that to witness the events of an infectious disease from its beginning to its end is a common experience to many observers.

The situation in the case of chronic diseases, which should in many cases no doubt be designated preferably diseases of long duration, is

*From the Department of Therapeutics, University and Bellevue Hospital Medical College of New York University, Third Medical Division of Bellevue Hospital and the Heart Committee of the New York Tuberculosis and Health Association.

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very different. Rheumatic disease of the heart is such a one. It is not often the opportunity of individual physicians to follow cases of this sort from onset to termination. Yet for many reasons, to do so is indispensable if knowledge of several sorts is to become available. That this disease is one, extending from what is frequently its stormy febrile beginning to an end having little apparent formal relation to it, required the observation of many decades to suggest. The fact seems now firmly established that there is a form of cardiac disease of which individuals die many years after the original rheumatic affection which occasioned it has completely disappeared. But what is scarcely understood is the fate of individuals in the intervening period and how long this period endures. Studies like this by Dr. DeGraff and Miss Lingg are, to all intents and purposes, pioneer works in elucidating the facts. In order that the facts should emerge, it was necessary to apply to them carefully defined terms, bearing on a variety of phases of this ailment. Once awareness was established of the phenomena which require recognition so as to measure the course of events unequivocally, clarity began to dawn. The duration of the various phases of rheumatic cardiac disease is becoming known. For this purpose the value of mathematical analysis has been learned. The error is often made that, in this connection, the use of statistical methods is an end in itself. Nothing can be further from the facts. Actually, the method is merely an instrument employed in the interests of description of the natural phenomena. But as an instrument it is invaluable, as these studies, and so many others in widely different fields of inquiry, amply demonstrate.

If it were not important to learn the history of this disease and of its various stages, first on its own account and second in order to judge of the health of patients and their ability in each of them, it would become of prime importance, nevertheless, to acquire this information in order to appraise the success of therapeutic procedures. Whoever has had experience in making such estimations knows the numerous logical difficulties involved in arriving at conclusions, even in simple situations. When the difficulties multiply, as they do in the case of diseases naturally of long duration, the complexity of analysis obviously increases. In any therapeutic enterprise in such situations almost the first question that requires answer concerns the influence of agent or procedure on *duration,* either of the disease as a whole or of any one of its phases. It makes a difference, furthermore, in which phase therapeutic interference is attempted. A second almost equally important question relates to the effect on the state of the patient's *health* in any one of the several phases of their illness. It is not a matter of indifference whether it is in the first or the last phase of so complicated a process in which a remedy is applied. It may matter,

furthermore, whether a consequence of instituting a procedure, an operation to excise the thyroid gland, for example, is a relief of disability or one which, although it does so, hastens on meanwhile the moment of the inevitable end. Other things being altogether equal, patients will wish perhaps to choose which is a preferable course for them.

The results of the present studies and of other similar ones which show so clearly the course of events in rheumatic cardiac disease and define so precisely the duration of each of its phases must, it seems, form the basis hereafter in appraising the success of any influence which is brought to bear upon it with the view to its modification. That the observation of many cases, each exactly studied, is necessary and the whole procedure of analysis difficult and time consuming is merely to state an inescapable fact; in no other way, in all likelihood, are convincing answers to be secured to problems which require urgently to be solved.

I

TO DESCRIBE rheumatic fever, especially its cardiac phase, is difficult because of its long duration. No one sees its beginning, middle, and end. Since the process of the disease is continuously active, an anatomical evolution takes place which it is extraordinarily difficult to reconstruct. To obtain a complete description, evidence of its various stages must be assembled piecemeal.

The problems presented by the extremely variable manifestations of rheumatic infection, particularly cardiac, make it necessary to study this disease from several points of view. Only by following this course can a proper description of its natural history, extending as it does over many years, be secured. The description must be based on three types of analysis.

First, its onset must be exactly known, and for this reason the types of initial infection, their incidence, their severity and certain other attributes, supplemented by bacteriological and immunological studies, must be described.

Second, the lesions must be described. These can now be identified. With this knowledge and the evidence from case histories, it may be possible to reconstruct the anatomical course of disease; though an account of the intermediate stages cannot escape being uncertain and fragmentary.

Third, patients must be observed throughout the course of the disease. To be successful the observations must be recorded so that they can be properly analyzed. Accurate description of this sort is the contribution which the Heart Committee of the New York Tuberculosis

and Health Association[1] is attempting to make. Since the facts dealing with the initial lesions and with the histological changes cannot always be secured, it has seemed advisable to lay emphasis on describing, as well as this can be done, the course of the disease.

For completeness of description all three methods are necessary. The use of the first facilitates recognition of the disease; the second establishes its anatomical criteria; and the third forecasts its course.

THE SAMPLE

A study of 1,633 cases of rheumatic heart disease was made.* The patients included were observed during the ten-year period 1921-1931. At the end of that time 644 (39.4 per cent) had died, 609 (37.3 per cent) were still living, and 380 (23.2 per cent) could not be traced. An analysis of the histories of the 644 dead has been completed and is now presented.

In a study of this nature success depends, as has been said, on the continuous observation of a large group of patients over a period of years. Loss of the records of many patients destroys the value of the sample remaining. The small group remaining is not necessarily representative of the total one. Failure to observe this simple principle is responsible for serious defects found in medical literature.†

The attempt was made to obtain after-histories of patients who could not be kept under continuous observation.‡ Many were traced and many were reexamined. Of others, interval histories and records of intercurrent illness and of treatment administered elsewhere were obtained in the uniform records kept in the heart clinics of New York City.[1] Many were traced through death certificates filed with the Bureau of Records of the Department of Health.§ By all these means, in the total group of 1,633 patients the fate of 73.3 per cent was learned; 80.7 per cent of those in the clinic, 71.3 per cent in the hospital ward, and 66.6 per cent of the private patients.

Those patients who were victims of a rheumatic infection but not subsequently of cardiac involvement are not included. Coombs[2] pointed out that 25 per cent of his rheumatic patients apparently recovered completely and showed later no clinical evidence of heart disease. Morse[3] found an even higher percentage (37 per cent).

The etiology was recorded as "unknown" in 193 (30 per cent), but mitral stenosis developed, nevertheless. Examinations post-mortem as well as clinical observations suggest that the etiology was rheumatic, though the initial infection must have been so slight as to have passed unnoticed. There is little evidence to support the view that mitral stenosis in the younger age groups can occur otherwise than in rheumatic infection. These patients are therefore included in this study.

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*The basic facts are derived from observations of patients in the adult cardiac clinic of Bellevue Hospital, the Third Medical Division of Bellevue Hospital and from private practices, recorded in a uniform manner on the charts provided by the Heart Committee of the New York Tuberculosis and Health Association, or, rarely, on the progress sheets of Bellevue Hospital. The practices of Dr. John Wyckoff and of Dr. Arthur C. DeGraff have been utilized for this purpose. We are indebted to Dr. Wyckoff for the use of many records and for his supervision of our analyses in many cases.

†For the opportunity of continuous observation of patients we are indebted to the social service staff of Bellevue Hospital.

‡For success in this effort we thank workers assigned to us by the Emergency Unemployment Relief Bureau.

§We are indebted to the Department of Health of New York, N. Y., for permission to make searches through death certificates.

Sex.—Among adult patients different observers report a slight predominance of males in rheumatic heart disease; but if children are studied, the ratio of females to males is reported as about 2 to 1 (Table I).[2, 4] The reason for the higher incidence of females in a group of children than in an adult group is partly explained later when the age at initial infection is discussed.

TABLE I

SEX

	MALES	FEMALES
DeGraff and Lingg (adults)	55.8%	44.2%
Davis and Weiss[12] (adults)	56.6%	43.4%
Cabot[7] (adults)	52.4%	47.6%
Coombs[2] (adults and children)	34.1%	65.9%
Wilson, Lingg and Croxford[4] (children)	38.8%	61.2%

Incidence of Other Etiological Forms of Heart Disease Complicating Rheumatic Heart Disease.—In 94.5 per cent heart disease was purely rheumatic. In 2.7 per cent the rheumatic lesion was complicated by the presence of either arteriosclerosis or hypertension, or both. In only 6 instances was rheumatic heart disease complicated by cardiovascular syphilis. All of these presented, in addition to disease of the mitral valve, aortitis or aortic insufficiency with a history of lues, or both.

Since patients with rheumatic heart disease die young, cardiovascular syphilis or the so-called senescent forms of heart disease rarely complicate these cases. In fact, most patients afflicted with rheumatic heart disease die before they reach the age at which the other two diseases are usually recognized. No cases of congenital heart disease appeared, chiefly because of the fact that this study deals with an adult group.

THE INITIAL INFECTION

Of chief importance is knowing the date of the initial rheumatic infection. The particular form of onset is not significant, but the lesion was defined strictly in conformity with the criteria published by the Heart Committee.[5] When there was doubt, the etiology was classified as *unknown*. It is probable that in some cases the *initial infection* represented reinfection, that the actual initial infection occurred earlier but was slight and escaped notice, as when discovery of heart disease antedated the recognition of the initial infection. The date of the first rheumatic manifestation is, however, the only landmark now available in describing the onset of rheumatic disease.

Age.—The range of the ages at which the first rheumatic manifestation occurred was wide, and spread from two to sixty-three years (Fig. 1*). The greatest incidence occurred in the decade from 10 to 19 years (39.6 per cent). The position of the *mode* at age 11 is particularly striking since the *mean* age is 17 years. In order to bring it to 17 years the initial manifestation occurred well beyond age 20

*Figs. 1, 2, 3, 4, 5, and 11 include only those cases in which the date of the first manifestation of infection was known.

in some patients. Eighty-four and seven-tenths per cent were infected before age 30 and only 4.4 per cent after 40 years. Obviously rheumatic infection is a disease of youth. Although a number of patients contracted heart disease in childhood, the series does not include those who died before they were old enough to appear in an adult clinic, usually 14 years. This must also be the case in the series reported by Grant,[6] in which analysis of the published case histories revealed a mean age at 18 and a mode at 10 years. By not including children who die before they are fifteen the mean age given for the occurrence of the initial infection is higher than it would be if all age groups were represented. Conversely, it is lower when the sample excludes patients whose initial infection occurs after age 14. This is the case in the

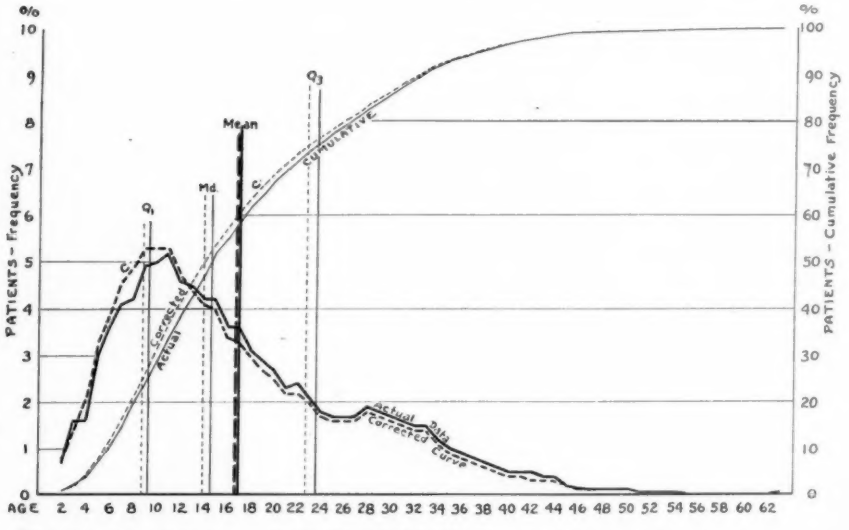

Fig. 1.—Age at first manifestation of infection.

The curves in this and most of the subsequent figures were smoothed by the method of moving averages and the statistical values read from the smoothed curves.

report published by Wilson, Lingg and Croxford,[4] who give a mean of 8 years. In order to arrive at a true mean, an estimate was made of patients who were excluded from this sample because they died before age 15.* The result places the median at 14 years (Fig. 1 C). The *mean* at 16.8 is only slightly lower than in the original curve,

*For this purpose Dr. Irving R. Roth was kind enough to allow us the use of data that he has collected in 598 cases of rheumatic infection in children at Mount Sinai Hospital, New York. An estimate of the number of cases lacking because of death before the age for admission to an adult clinic was made by using the following relationship, A:C::B:X, when A is the age of the Mount Sinai patients alive after age 14; B is the age of our series less those dead before age 15; C is the age of the Mount Sinai patients dead before age 15; and X is the calculated age of patients who would have been included in our series had they not died before reaching the age of 15 years.

The value of X was determined for each age from 1 to 14. The data were added to the original distribution. The new curve (Fig. 1 C) now includes patients who, it is estimated, died before reaching the fifteenth year.

but the *mode* is flatter and falls earlier, at 9, 10 and 11 years, closer to that of 8 years reported by Wilson, Lingg and Croxford.[4] The chances of developing initial rheumatic infection are greatest in the age group 9 to 11 and decrease yearly after that. At the same time the *mean* age at onset of rheumatic infection is not so early in childhood as many pediatricians have supposed. It appears that, when a group is not confined to children, about 30 per cent develop their first infection beyond the adolescent period.

Sex.—The age at onset differs in the sexes. To about age 13 years girls predominate over boys. From 13 to 28 years the incidence is about the same for both. Afterward men are more likely to develop rheumatic infection leading to heart disease (Fig. 2). This may explain the higher ratio of females among children, and of males among

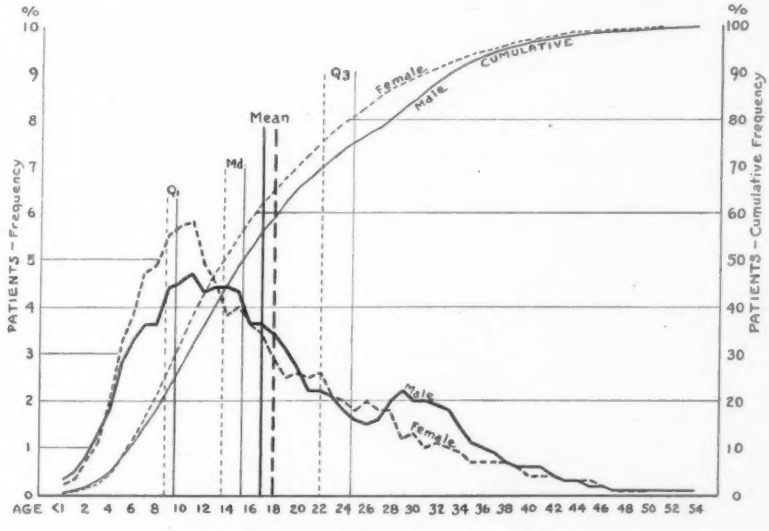

Fig. 2.—Age at first manifestation of infection by sex.

adults referred to above. It may also explain Cabot's[7] statement that the disease seems to begin earlier in males, since his data represent chiefly older patients.

DURATION OF DISEASE

The virulence of the infection and the degree of myocardial damage produced are extremely important factors in the duration of the disease. Whether such factors can be measured is questionable. It is a common belief, for instance, that repeated attacks of rheumatic fever lead to earlier fatality. Yet Willius[8] and, recently, Friedberg and Tartakower[9] found that there is no constant relation between the number of attacks of rheumatic fever and the time when death occurs. An attempt to find such a relation was abandoned when no absolute

criteria for rheumatic activity could be established, nor could the degree of activity be classified. Even if these factors could be correctly appraised, it is only over long periods of time in a home or in a hospital that the desired information could be obtained. These factors then, although important, must be left out of consideration.

The mean duration of life, from the onset of rheumatic infection to death, was found to be 15 years. Although some patients lived much longer, one as long as 58 years, such experiences are rare; 75 per cent lived for less than 23 years after onset (Fig. 3). It may be said, then, that a patient has only an even chance of living 12 years, and only one chance in five of living as long as 25 years after initial infection.

The mean duration of life in this series is very much shorter than the 30 years estimated by Coombs.[2] He analyzed two groups. His

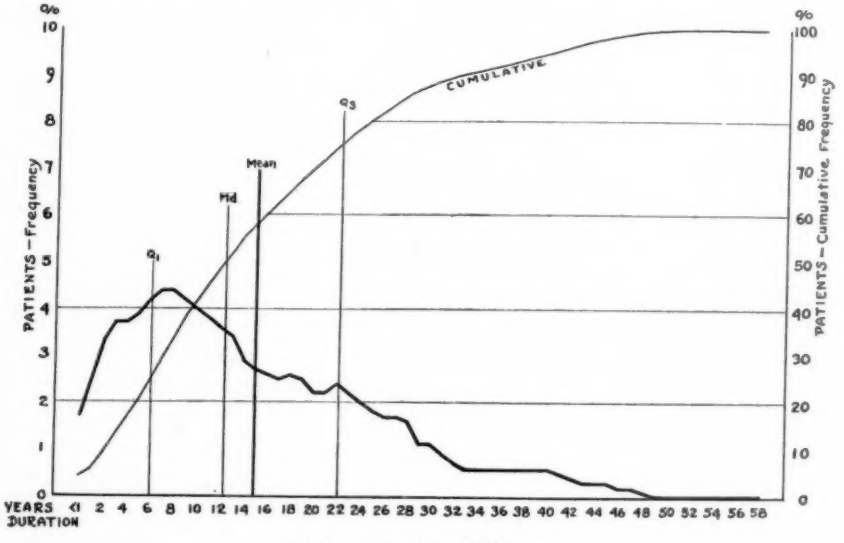

Fig 3.—Duration of disease.

first comprised patients seen very close to the date of onset and followed to an average age of about 25 years; the second, those who presented heart disease when they first came under observation and who had reached at that time an average age of 25 years. By linking the first group to the second he estimated the duration of life to be 30 years. It is obvious that such methods and conclusions are unsound. Willius,[8] using much the same technic as is used in this report, with a similarly constituted sample, arrived at a mean duration of life of 14 years, which compares well with 15 years in the series here presented.

Grant,[6] although he says that "it is apparent from this study that the outlook for patients suffering from valve defect is not so bad as

it is generally thought," states that "within 10 years, 473 or about half the cases have died." A word should, perhaps, be said concerning Grant's method of analysis, since without pointing out the differences between his and our presentation, reference to his conclusions in comparison with those presented in this report may lead to misunderstanding and confusion.

In the first place, Grant's sample consists of 1,000 ex-service men. It is limited to the male sex; it is limited to individuals at or above the recruiting age, and therefore, like our sample, excludes those patients with rheumatic heart disease that do not survive to adult life. It excludes also those who may have been rejected for military service because of cardiac damage, the degree and its definition varying during the course of the war; being limited to *ex-service* men (none came under observation until 1919 when the war was over), it excludes men who may have been recruited in spite of damaged hearts, and yet may not have outlived the strain of military service. The sample, then, is not representative of rheumatic heart disease among males, as a whole; it is not representative even of adult males but is limited to the better risks in the class selected for study. One should expect naturally, therefore, to find in this group of patients a more favorable prognosis than is usual in this disease.

In the second place, he relates prognosis not to any definite event in the course of the disease, but rather to the time when patients happened to come under his observation. This time, quite obviously, does not represent the same stage in the course of the disease in all patients. Statements made in his conclusions, such as, "Fifty-one per cent are known to be alive"; "Forty-seven per cent are known to have died"; or "Auricular fibrillation, present originally in ten per cent, develops later in eight per cent," have, therefore, little bearing, being related in his treatment of the problem to the time of *his* contact with the cases, on the calculation of prognosis.

In the third place, he states his conclusions in terms of valvular disease as a whole, in spite of the fact that this includes two entirely distinct processes of disease, rheumatic as well as syphilitic. His statement that "in a fair sample of the adult male population of the country . . . . we see that aortic regurgitation is more common than mitral stenosis and that of all the valve defects syphilitic aortic regurgitation is the most frequent" is not in accordance with reported experience in this country, in which even among adult males rheumatic valvular disease is more common than syphilitic aortic insufficiency. Grant classifies cases of mitral stenosis with or without aortic regurgitation, in the absence of a definite history of rheumatic fever, in a separate rubric "indefinite etiology," even though he believes these cases to be rheumatic. If his table is rearranged and these cases

are included in the rheumatic rubric, it is mitral stenosis which stands out as a more frequent lesion than syphilitic aortic regurgitation.

In studying prognosis Grant divides his cases according to etiology and, furthermore, according to various valvular lesions or combinations of lesions. This method reduces the groups to such small numbers that an estimation of prognosis becomes difficult. There is, however, another difficulty; it is desirable to know the difference in prognosis between syphilitic and rheumatic heart disease without regard to which valve is involved. This analysis Grant has not made. Since he has published summaries of his case histories, we have been enabled to retabulate his data in order to make them comparable to those now presented. Subsequent references to Grant in this paper are based, for the most part, on our own analyses of his data. These reveal, among his deceased rheumatic patients, a mean duration of life of 19 years. Seventy-five per cent lived for less than 26 years. This somewhat longer duration of life than was experienced by the group now studied may be explained by the method of selection of his patients to which reference has already been made.

A similar explanation may be applied to the results published by Friedberg and Tartakower.[9] They give as a mean duration of life 23 years after first infection in one group (63 cases) and 38 years in another group (29 cases) of patients that presented rheumatic heart disease both clinically and at autopsy. These groups include no patients who contracted the disease before puberty, and the second group comprised not only particularly long lived individuals, but also patients whose heart disease was discovered accidentally, who at no time experienced symptoms of cardiac insufficiency. Unfortunately they did not publish the age distribution of these two groups of patients at the time they first observed them. If, as is implied, they were beyond 30 years of age at that time, so that patients who succumb to the disease before that age are excluded, a mean duration of disease would occur among them that is much longer than would be the case if the sample were not so biased. The fact that the number of cases in these groups is so small and that the mean age at death is as high as 41.8 years, leads to the belief that our deduction is correct. In the series here presented, for example, 46 patients lived for 30 or more years after onset of infection (Fig. 3). If we computed the mean duration of disease in this group, it would exceed 30 years.

The age at the time of initial infection has an important bearing on the duration of life. In general, the younger the patient at first infection, the longer is the interval before death (Fig. 4). This corroborates the experience reported by Willius[8] and by Friedberg and Tartakower.[9] It is contrary to the experience of pediatricians[4] who report an unfavorable prognosis among children when the disease

starts early. Such cases are, however, not included in this sample. In view of these observations, inferences as to prognosis must not be drawn without considering the fact that with advancing age life expectancy decreases even among normal individuals. This was also pointed out by Friedberg and Tartakower.[9]

According to Cabot[7] the duration of rheumatic heart disease is shorter in men than in women. In this series, as also in the two groups studied by Friedberg and Tartakower,[9] there is, however, no difference. The curves can almost be superimposed.* For males, the mean duration is 14.9 years, for females 15.0 years; the median is at 12 years and the first quartile at 6 years for both sexes, and the third quartile at 22 years for males and between 20 and 21 years for females.

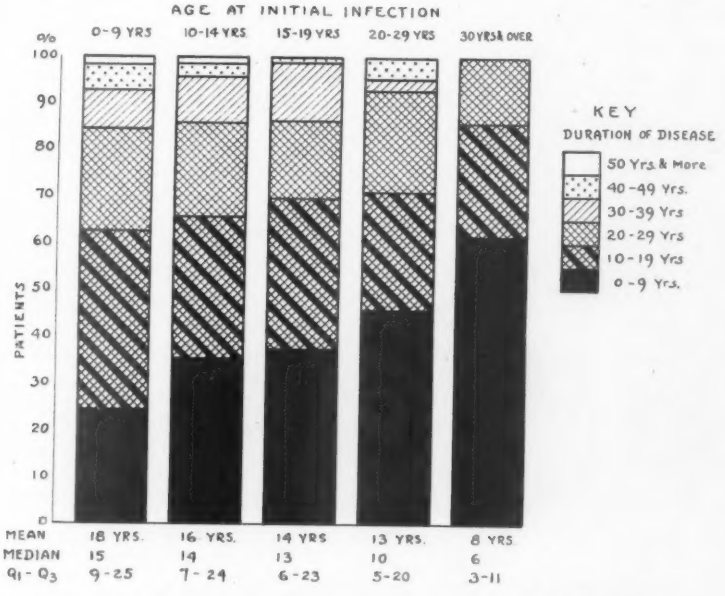

Fig. 4.—Duration of disease related to age at initial infection.

CARDIAC INSUFFICIENCY

The date at which a patient affected with rheumatic fever begins to suffer from impairment of his heart is an important landmark. Increasing fatigue and dyspnea on effort constitute the chief evidence. Other causes such as anemia and thyrotoxicosis must be excluded. The clinical phenomena are such as change a patient from Class I to IIA or IIB.†[5]

Onset of Symptoms.—Symptoms of cardiac insufficiency were experienced by nearly all patients (96.2 per cent). The mean interval be-

*Space does not permit publication of these curves.

†Provided, of course, that the functional disability was due to cardiac insufficiency.

tween the onset of infection and the first clinical evidences of cardiac insufficiency was 11 years. It is noteworthy that 22.9 per cent of the patients presented symptoms within a year after the first manifestation of infection (Fig. 5). In more than one-half the patients, the interval free from symptoms was less than 10 years.

Analysis of Grant's[6] records places the mean interval between onset of infection and the beginning of cardiac symptoms likewise at 11 years; Romberg[10] found it to be 7 years in two-thirds of his cases and longer in the rest; Friedberg and Tartakower[9] 19.6 years in their first and 33.9 years in their second group. If, as we suspect, their series are made up of the more fortunate survivors, this longer period of good cardiac reserve may be explained.

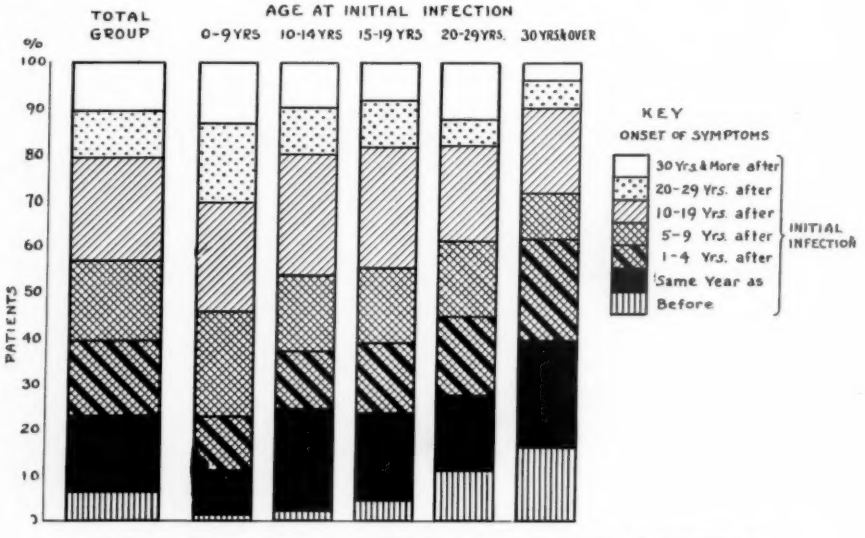

Fig. 5.—Interval between initial infection and onset of symptoms.

As might be expected from the data already presented on the duration of life, the older the patient when he is first afflicted with rheumatic infection, the shorter is the interval before cardiac symptoms make their appearance (Fig. 5).

There is a small group in which symptoms of cardiac insufficiency occurred before the onset of initial infection (Fig. 5). It is possible that in these patients the symptoms were not due to cardiac insufficiency. On the other hand, it may be, as has been stated, that the age given as that of the initial infection is incorrect and preceded the age obtained. This is especially likely among individuals said to be infected after the second decade. In every case the attempt was made to find the earliest evidence of cardiac insufficiency. It is not likely that errors were made in many instances, for the intervals between the appearance of symptoms of heart failure and death were short.

Once patients complained of symptoms of cardiac insufficiency, life expectancy was brief. The mean duration of life was five years. Fifty per cent died within from three to four years after symptoms first appeared (Fig. 6).

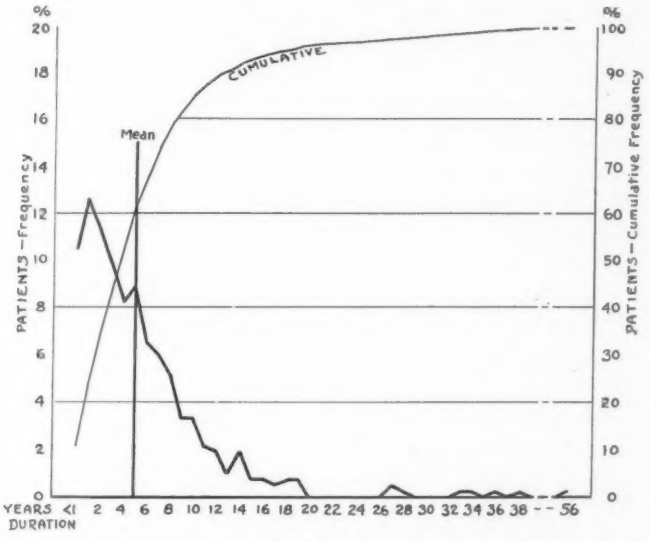

Fig. 6.—Duration of life after onset of symptoms.

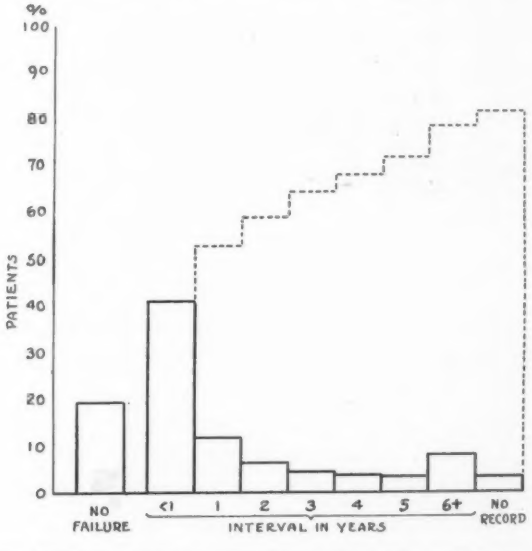

Fig. 7.—Interval between onset of symptoms and first attack of heart failure.

Heart Failure.—Heart failure has been taken to exist when the symptoms of cardiac insufficiency are so pronounced that patients are unable to do any work, but go to bed and remain there for some time. Heart failure may be due to many different causes, among them rheu-

matic infection itself. An attempt was made to ascertain the cause of failure in each case, but this was unsuccessful—probably because of the lack of proper criteria.

About 80 per cent suffered at least one attack of heart failure (Fig. 7). In general, patients began to experience attacks of heart failure about two years after symptoms of cardiac insufficiency had made their appearance. In the remaining 20 per cent either its occurrence was not recorded or the data were inadequate. Of the latter a few may have experienced heart failure before death. This group includes, however, those patients in whom the natural course of rheumatic heart disease was shortened by one of the fatal complications, such as cerebral embolism, subacute bacterial endocarditis, or an intercurrent infection.

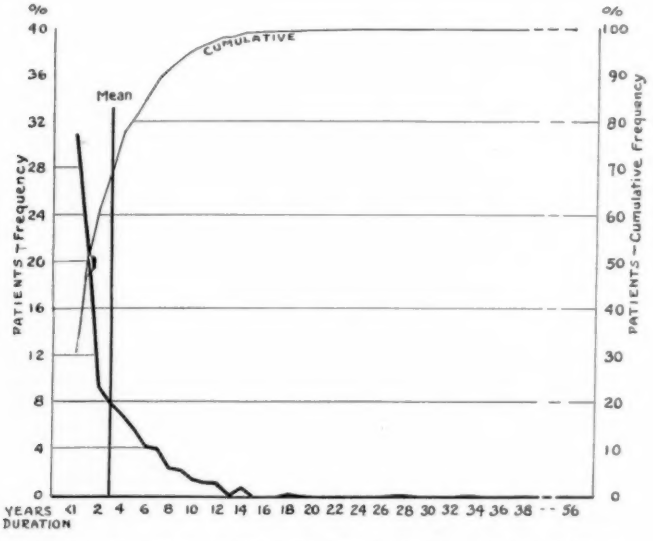

Fig. 8.—Duration of life after first attack of heart failure.

Duration of Life After First Attack of Heart Failure.—The mean duration of life after the first attack of heart failure was three years; in 75 per cent less than five years (Fig. 8). On the basis of this experience, the chances that a patient will be alive one year after the onset of heart failure are even; the chances that he will be alive five years are 1 to 4. The experience of Friedberg and Tartakower[9] was similar to this; the mean duration was 2.5 years, and one-third of the patients lived for only one year. When Grant[6] says that prognosis depends on "the degree of cardiac enlargement and the grade of cardiac failure, as estimated first by exercise tolerance and secondly by the presence of venous congestion," he says in effect what is pointed out here; namely, that once a patient is in heart failure, his course is almost run.

DEATH

Age at Death.—The mean age at death was 33 years, the median about the same and the interquartile range extended from age 23 to 42 years (Fig. 9). Study of this group of 644 patients leads to the conclusion that although it is possible for patients to live for years, even beyond 70, three-fourths do not survive much beyond age 40, and about half are dead before 33 years. If patients contract the disease in adult life or survive the first two decades of life, death is most common between ages 30 and 39 (30 per cent); in the first half of this decade 15.2 per cent died, more than in any other 5-year period. Only about 10 per cent survived the fifth decade (Fig. 9). This distribution is practically the same as that found by Cabot,[7] Willius,[11]

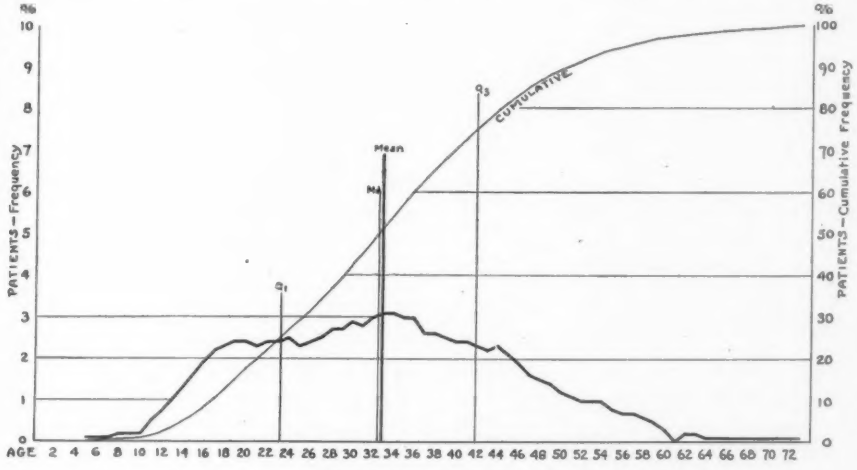

Fig. 9.—Age at death.

and Grant.[6] A study of Grant's[6] data places the mean age at death at 36 years; three-fourths died before age 43 was reached. Recently Davis and Weiss[12] published a similar analysis. In order to make the two groups exactly comparable those cases in the present report were tabulated separately in which death was due to heart failure; the mode again fell in the fourth decade, and less than 10 per cent of patients survived the fifth decade (Table II). When the age at death from causes other than heart failure was considered, a mode was found in the third decade, but at the same time nearly 15 per cent survived the fifth decade. The higher age at death (37 years) in Davis and Weiss's[12] cases cannot, therefore, be explained by their selection of cases to exclude causes of death other than cardiac. The difference between their figures and Cabot's and these probably has something to do with the original sampling.

TABLE II

AGE GROUPS	DAVIS AND WEISS	DE GRAFF AND LINGG		
		DEATHS DUE TO		
	DEATHS %	HEART DISEASE %	HEART FAILURE %	CAUSES OTHER THAN HEART FAILURE %
0- 9	3	1.1	0.7	–
10-19	17	16.4	16.6	11.6
20-29	12	23.3	22.8	28.2
30-39	21	29.2	30.8	27.1
40-49	24	21.2	20.0	18.2
50-59	13	7.1	7.3	12.1
60-69	10	0.9	1.1	2.8
70-79	–	0.7	0.7	–
Mean	37	32.6	32.7	34.2
Median	38	33.0	33.0	34.0
Q_1	24	23.0	23.0	25.0
Q_3	50	42.5	42.5	44.5

The method of sampling may also explain the figures published by Friedberg and Tartakower[9] who give 53 years as a mean age at death. They state that although the duration of life after first infection decreases as the age at initial infection increases, the age at death remains the same, regardless of when the onset of infection occurs. The same inference could not be drawn from a study of this series. The decade claiming the greatest number of deaths was always the decade following that in which initial infection occurred (Fig. 10).

Fig. 10.—Age at death related to age at initial infection.

Causes of Death.—Causes of death were divided first into two general groups, those due to heart disease and those due to some other cause. In many cases it was possible further to subdivide the cardiac deaths. Death was usually due to heart disease (74.2 per cent), the largest group (45 per cent) dying of congestive heart failure, and 5.6 per cent dying of bacterial endocarditis. A diagnosis other than

"heart disease" was impossible in 23.6 per cent. Embolism, infarction or thrombosis and other diseases claimed, respectively, 9.2 per cent and 9.9 per cent. Among patients suffering from rheumatic heart disease the chances of dying a cardiac death are therefore 3 to 1, and the chances of dying of other diseases not referable to the circulatory system are 1 to 9.

The presence of certain conditions in the course of rheumatic infection which eventually lead to death shortens the duration of life in varying degrees. In the case of subacute bacterial endocarditis, for example, 23 of 28 patients died within 14 years, and 15 (50 per cent) within less than 8 years. In pneumonia as a cause of death a comparable situation is present. Of 13 patients, 8 died within 14 years. Of 21 patients the subject of embolism 12 died in less than 13 years. *The Medical Impairment Study* published in 1929 by the Actuarial Society of America and the Association of Life Insurance Directors[13] indicated rather broadly that shortening of life expectancy by complications such as have been noted may be expected.

DISCUSSION

It is possible that in confining the analysis of the course of disease to the 644 patients who died, the usual course of the disease has been placed in a most unfavorable light. In order to discover whether this is the case, we analyzed briefly the records of the 609 patients who were known to be alive in 1931.

As a group, these living patients were somewhat younger (about 5 years) when they first came under observation. They were about 2 years younger when first infected. The duration of disease, so far, has been slightly less (mean 14 years, median 12 years, quartiles 9 and 21 years). Only 183 (30 per cent against 80 per cent) have, however, so far developed heart failure, but their duration of life has already been longer (mean 17 years, median 16 years, quartiles 9 and 24 years). In the remaining 70 per cent (426 patients) the life span of the disease has so far been about 2 years less than in the group that died (mean 13 years, median 10 years, quartiles 6 and 17 years). It is possible that the fact that those still living were younger at the time of initial infection accounts for their slightly greater longevity.

Unfortunately there is here no conclusive evidence that can be brought to bear on the question raised. Whether the 644 cases studied present the normal or more unfavorable course of disease, and if so, to what degree, must remain a matter of conjecture. The period, that is to say the calendar year, in which infection was acquired may be determining in its course. The effort will be made to study the subsequent histories of the patients still alive.

SUMMARY AND CONCLUSIONS

The course of rheumatic heart disease, based on the 644 patients who are dead in a total of 1,633 patients coming under observation in the 10 years up to 1931, has been described. Of these patients 55.8 per cent were males and 44.2 per cent were females. Rheumatic heart disease usually existed alone (94.5 per cent) and was seldom combined with other etiological types (5.5 per cent).

It is readily seen that this disease is in the main one of childhood and early adult life, for it occurs and runs its course chiefly within

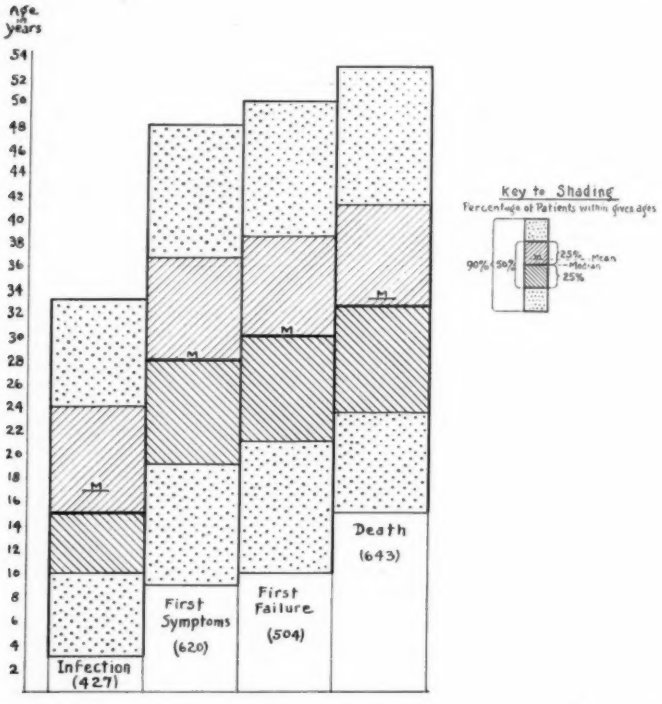

Fig. 11.—Age at occurrence of initial infection, first cardiac symptoms, first attack of heart failure, and death.

How to read chart. **Example: The median age of patients at the time they were first infected is 15 years (indicated by heavy black line across first column); 50 per cent of the patients were first infected between ages 10 and 24; 25 per cent between 10 and 15 (indicated by diagonal shading); 90 per cent were infected between the ages 3 and 33 (indicated by stippled shading).**

the first four decades. After age 40 there is a small proportion of sufferers. Three-fourths of those who survived to adult life are already dead. The average age at initial infection is 17 years; at the first symptoms of cardiac insufficiency 28 years; at the first appearance of heart failure 30 years, and at death 33 years (Fig. 11). Stated in another way, the average patient is infected at age 17, but will be free from symptoms and able to carry on ordinary physical activity

for 11 years. He will then begin to suffer from diminished cardiac reserve culminating in heart failure 2 years later. From this time to death, 3 years later, he is wholly an invalid or at least, in most cases, seriously incapacitated. The period of economic usefulness of a person afflicted with rheumatic heart disease is, on the average, not more than 11 years after initial rheumatic infection; in most cases less than 9 years. Once symptoms of cardiac insufficiency appear, heart failure and death follow rapidly. Fifty per cent suffer their first symptoms and failure and die within a period of from 16 to 20 years, or between 20 and 40 years of age, the years of early maturity. To see even terminal stages of this disease after the age of 50 years is not a common experience.

Death usually occurs as a result of a failing heart, but life is shortened in a fair proportion of cases by such conditions as subacute bacterial endocarditis, pneumonia, and other diseases.

The authors wish to express their indebtedness to the many doctors who have worked week after week for many years in the Adult Cardiac Clinic at Bellevue Hospital and by their work have made possible the accumulation of information that has been used in this paper.

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THE COURSE OF RHEUMATIC HEART DISEASE IN ADULTS*†‡

II. The Influence of the Type of Valvular Lesion on the Course of Rheumatic Heart Disease

Arthur C. DeGraff, M.D., and Claire Lingg, M.A.
New York, N. Y.

IN A previous paper the course of rheumatic heart disease from onset to death in 644 patients was described. Certain aspects of the disease were analyzed, but a discussion as to how the various valvular lesions modify its course was reserved for this paper. Reference should be made to the previous paper[1] for the source of the data and the methods of analysis employed.

The best approach to a description of the influence of the valves affected on the course of this disease may be that of a pathologist. For this reason de la Chapelle, Graef and Rottino[2] studied the cases which came to autopsy during thirteen years from the Third Medical Division of Bellevue Hospital. The difficulty with this method is that the number of cases with adequate clinical records becomes too small for proper analysis. Only 119 cases were found suitable. For prognostic purposes it is desirable to establish signs descriptive of an underlying lesion. Signs were established in the 644 cases now presented. Clinical records are available in 45 per cent of the patients studied post-mortem by de la Chapelle, Graef and Rottino. Although only 13 per cent of the total number came to autopsy, the study of these served to illustrate the degree of closeness with which clinical and post-mortem diagnoses corresponded.

The diagnostic criteria employed were those of the Heart Committee of the New York Tuberculosis and Health Association;[3] accuracy of diagnosis was assured by insisting upon complete studies in each case.§ There is probably a difference in the degree to which various valvular lesions can be accurately diagnosticated. For example, mitral stenosis can with care be recognized ultimately in nearly every instance. Concerning other valvular lesions, the criteria are, however, not so clear,

*From the Department of Therapeutics, University and Bellevue Hospital Medical College of New York University, Third Medical Division of Bellevue Hospital and the Heart Committee of the New York Tuberculosis and Health Association.

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§We are indebted to Dr. John Wyckoff and to other members of the staff of the cardiac clinic of the Third Medical Division (New York University) of Bellevue Hospital for this aid.

and errors are more likely to occur. The error is probably greatest in deciding on the presence of tricuspid and pulmonic lesions (Table I).

TABLE I

CLINICAL AND POST-MORTEM DIAGNOSIS OF VALVULAR LESIONS

VALVULAR LESIONS	PERCENTAGE OF CASES IN WHICH POST-MORTEM DIAGNOSIS AGREED WITH CLINICAL DIAGNOSIS
Mitral stenosis	95
Aortic lesions	58
Tricuspid or pulmonic lesions	15

INCIDENCE OF TYPES OF VALVULAR LESIONS

The mitral valve, as has been pointed out by other observers, was found to be most frequently affected. Painstaking anatomical studies have shown that the mitral valve is involved in almost every case of rheumatic heart disease. Coombs[4] found evidence of this injury in every one of 97 cases, and in the cases at the Bellevue Hospital it existed in all but a few instances.[2] Yet, clinically, slight valvulitis may cause little or no detectable incompetence or stenosis.

Mitral stenosis, usually combined with mitral insufficiency but with no other valvular lesion, was recognized clinically in 62.5 per cent (402) of cases. This incidence is practically identical with that found post-mortem by de la Chapelle, Graef and Rottino,[2] but is higher than that reported by Cabot[5] and that computed from data published by Grant[6] and lower than that reported by Willius[7] (Table II).

TABLE II

INCIDENCE OF VALVULAR LESIONS

LESION	DEGRAFF AND LINGG	CABOT	WILLIUS	GRANT
Mitral stenosis	62.5%	51.5%	77.0%	44.0%
Mitral and aortic lesions	28.6%	19.2%	9.3%	39.2%

Combined mitral and aortic lesions were recognized in 28.6 per cent (184) of cases. This is higher than the figure reported by Willius[7] and by Cabot,[5] but lower than that calculated from Grant's[6] reports (Table II). Five of the 184 patients were infected also with syphilis. In such cases it is impossible to tell, clinically, whether aortic insufficiency is luetic or rheumatic; but the probability of its rheumatic origin, certainly in the presence of organic mitral disease, is very strong. Even if these five cases were omitted, however, the incidence would be higher than that either of Cabot[5] or of Willius.[7] Mitral or aortic lesions complicated by pulmonic or tricuspid lesions occurred in 29 (4.5 per cent) instances.

The incidence of other valvular lesions was small. The relative rarity of mitral insufficiency (12 cases, 1.8 per cent) alone has already been pointed out by Cabot.[5] The very low incidence of aortic insufficiency (8 cases, 1.2 per cent), unaccompanied by other valvular lesions, is not the experience of other observers. It is possible that cases of pure aortic insufficiency were included among those of combined mitral stenosis and aortic insufficiency, especially if a Flint murmur were mistaken for the murmur of mitral stenosis. It is also possible, on the other hand, that cases of pure aortic insufficiency not of rheumatic origin may have been classified by other observers as rheumatic. That this is not improbable is borne out by experience in anatomical postmortem diagnosis at Bellevue Hospital,[2] according to which uncomplicated rheumatic aortic insufficiency was found to be rare; its incidence was, in fact, similar to that found clinically. Aortic stenosis accompanied aortic insufficiency in combined mitral and aortic lesions in 39 cases. In 9 patients (1.4 per cent) valvular lesions appeared in acute terminal carditis, death occurring before a diagnosis of chronic valvular disease could be made.

Incidence of Types of Valvular Lesions by Sex.—Although more males (55.8 per cent) than females (44.2 per cent) appear to be afflicted with rheumatic valvular disease,[1] mitral valvular disease seems for some reason to be more common among females (76 per cent as against 58 per cent). Disease of the aortic valve appears, on the other hand, to be twice as common among males (40 per cent as against 22.8 per cent[5, 7, 8]).

TYPE OF VALVULAR LESION RELATED TO AGE AT ONSET OF INFECTION

Patients who are infected early, in the first decade, are more likely to develop aortic, and even tricuspid and pulmonic, lesions (49.5 per cent against 34.9 per cent). Among individuals infected later, uncomplicated mitral stenosis is more common (60 per cent as against 45 per cent). Aside from this apparent trend no other significant relationship was noted.

TYPE OF VALVULAR LESION RELATED TO DURATION OF DISEASE

The valve involved seems to exert no influence on the duration of life with the exception of the pulmonic and tricuspid valves, which render prognosis slightly less favorable (Fig. 1). The small number of cases of pure aortic lesions forbids the drawing of conclusions. An attempt is made later, under causes of death, to explain the apparently unfavorable prognosis in cases of uncomplicated mitral insufficiency. Patients with aortic stenosis are regarded by Cabot[5] as the longest lived in the rheumatic group, but he based this conclusion apparently on age at death and not on duration of disease. It has long been known

that aortic stenosis without other valvular lesions is relatively common in older people, but its origin, whether degenerative or inflammatory, is obscure. If inflammatory, it must be considered, it is said, as rheumatic. Only one such case was found, and this patient lived for twenty-five years after the onset of disease.

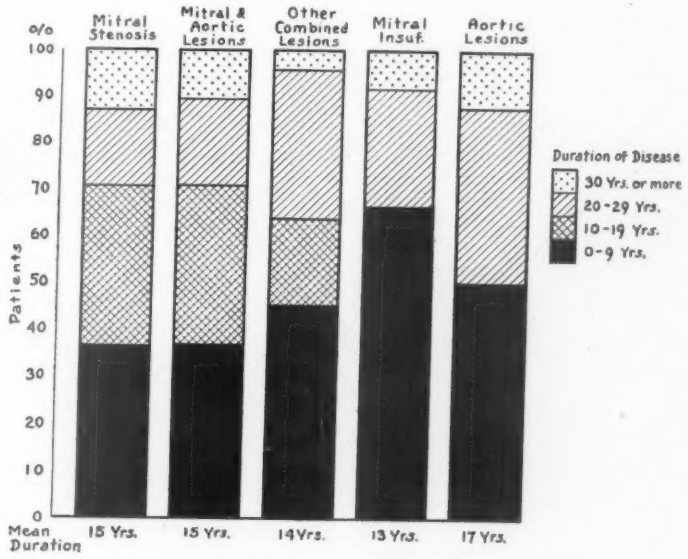

Fig. 1.—Duration of disease by valvular lesions.

Both Cabot[5] and Willius[7] reported a considerable difference in the duration of life depending on which valve was affected (Table III), but Friedberg and Tartakower[9] did not regard the nature of the valvular lesion as of primary importance in prognosis.

TABLE III

TYPE OF VALVULAR LESION RELATED TO DURATION OF LIFE

	LESIONS		
	MITRAL STENOSIS	MITRAL AND AORTIC	AORTIC
Willius[7]	12 yr.	16 yr.	22 yr.
Cabot[5]	15 yr.	3 yr.	–
DeGraff and Lingg[9]	15 yr.	15 yr.	17 yr.

TYPE OF VALVULAR LESION RELATED TO SYMPTOMS OF CARDIAC INSUFFICIENCY

The type of valvular lesion does not influence the *time* of development of symptoms of cardiac insufficiency. The average interval after the onset of the initial infection was about the same regardless of the type or number of valvular lesions (Table IV). Nor does the type of lesion appear to make much difference in duration of life after the

development of symptoms except in the case of aortic lesions. The small number of patients in this class renders inference of little value (Fig. 2).

TABLE IV

INTERVAL FROM INITIAL RHEUMATIC INFECTION TO FIRST SYMPTOMS OF CARDIAC INSUFFICIENCY

VALVULAR LESIONS	MEAN	MEDIAN	$Q_1 - Q_3$
Mitral stenosis	10 yr.	7 yr.	Less than 1 yr. to 15 yr.
Mitral and aortic	9 yr.	5 yr.	Less than 1 yr. to 15 yr.
Aortic	9 yr.	6 yr.	Less than 1 yr. to 11 yr.

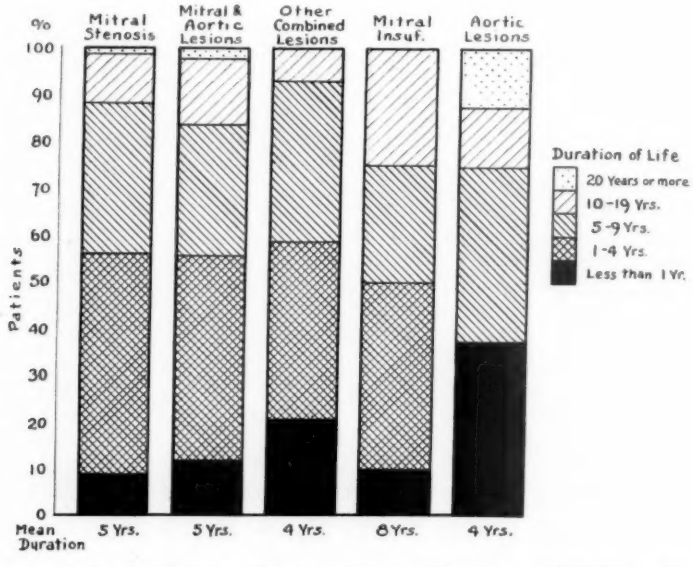

Fig. 2.—Duration of life after onset of symptoms by valvular lesions.

TYPE OF VALVULAR LESION RELATED TO CONGESTIVE HEART FAILURE

Heart failure with congestion appeared at about the same time (mean age 31 or 30) whether mitral stenosis or mitral and aortic disease was present. In the aortic group, it appeared earlier if it appeared at all, but more than one-third escaped congestive heart failure altogether, as far as is known, and the remainder is too small to warrant analysis. The average duration of life after the appearance of heart failure in mitral stenosis and in mitral plus aortic disease was brief (Fig. 3). In aortic lesions it was longer (7 years), but here again, because of the small number of cases, conclusions drawn now would be misleading.

The mean duration of life in patients with mitral insufficiency, after the appearance of congestive heart failure, was less than one year, but there were only 12 cases altogether.

CAUSE OF DEATH RELATED TO TYPE OF VALVULAR LESION

Death was usually due to some form of cardiac disease. In mitral stenosis, 70 per cent, in mitral and aortic valvular disease, 79 per cent, in disease of the tricuspid or pulmonic valve, 90 per cent, and in aortic valvular disease 75 per cent of the patients died cardiac deaths.

Congestive heart failure was the type of cardiac death most frequently seen, especially when the pulmonic or tricuspid valve was involved (in 83 per cent), but a little less often when only one valve was diseased, as, for example, in aortic insufficiency (25 per cent) and in mitral insufficiency (25 per cent). In the former, however, 75 per cent died cardiac deaths; in the latter only 41.6 per cent, while one-

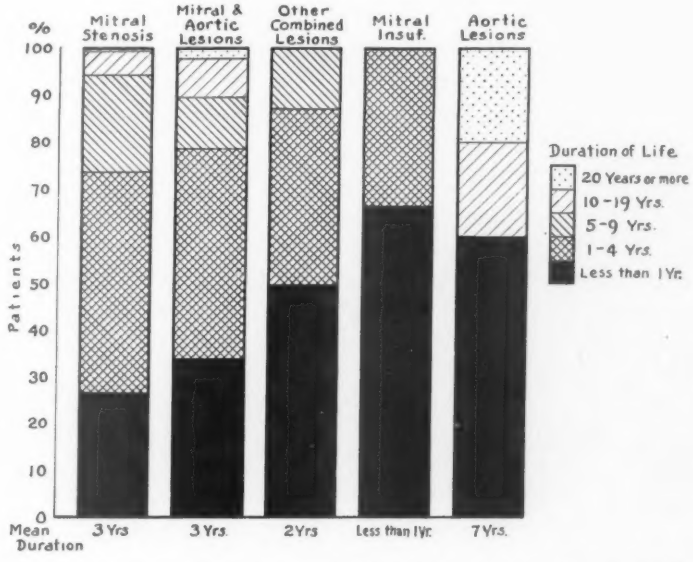

Fig. 3.—Duration of life after onset of heart failure by valvular lesions.

third died of other diseases, a much larger proportion than in any of the other groups. This may explain the apparently unfavorable prognosis already referred to.

It appears then that whereas among patients suffering from rheumatic heart disease the chances of dying cardiac deaths are in general 3 to 1, in mitral insufficiency they are only 1 to 1.4, and the chances of dying of other diseases not related to the circulatory system are 1 to 2. Slightly fewer patients with mitral stenosis died in congestive failure than patients suffering aortic disease combined with mitral stenosis (42 per cent against 48 per cent). The chances of developing congestive failure are greater, it seems, the greater the number of valvular lesions.

In agreement with other observers,[10-15] we found that subacute bacterial endocarditis was an infrequent cause of death in uncomplicated mitral stenosis (9 cases). It occurred more often when the aortic valve was diseased (16 cases).

SUMMARY AND CONCLUSIONS

An analysis of the effect of the type of valvular lesion on the course of rheumatic heart disease has been presented, based on the records of 644 patients who died. The importance of using for analysis data obtained during the life of the patient rather than the records from autopsies has been discussed. The incidence of the various valvular lesions is given. Mitral valvular disease was found to be more frequent in women, whereas aortic disease was approximately twice as frequent in men. The age at initial infection seemed to influence the type of subsequent valvular lesion only so far as the first decade of life is concerned. In a larger proportion of patients infected before age 10 than among those infected later in life, more than one valve was affected. The valve affected did not seem to influence the duration of life except in the case of the pulmonic or tricuspid valves. In the presence of damage to these, prognosis became slightly less favorable than when mitral stenosis appeared either alone or in combination with aortic lesions. In considering the relatively short duration of life observed in cases of mitral insufficiency alone, the high incidence of deaths due to other than cardiac or circulatory diseases must be taken into account.

The interval from initial rheumatic infection to the appearance of symptoms of cardiac insufficiency or congestive heart failure and the subsequent duration of life were about the same regardless of the valve or the number of valves affected.

Most of the patients died cardiac deaths, the incidence apparently being higher the greater the number of valvular lesions. Congestive heart failure appeared more frequently as a cause of death when disease of more than one valve was present; and subacute bacterial endocarditis when the aortic, tricuspid or pulmonic valve was diseased.

The evidence here presented lends support to the statements made by Flint[16] in 1862, by Mackenzie[17] in 1925, and more recently by Grant,[6] that valvular disease in itself gives no information as to prognosis.

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RHEUMATIC HEART DISEASE

IV. The Life History of the Severe Form of the Disease*

David Davis, M.D., and Soma Weiss, M.D.
Boston, Mass.

CLINICAL DURATION OF RHEUMATIC INFECTION

KNOWLEDGE of the time of onset of rheumatic infection and the age at death is essential in a study of the life history of rheumatic heart disease. In previous communications the age distribution at death in a group of patients with rheumatic heart disease was presented.[1, 2] Corresponding statistical data showing the onset of the rheumatic infection leading to heart disease are difficult to obtain because of the well-recognized fact that advanced cardiac damage not infrequently occurs without any recognized clinical manifestation of the rheumatic infection, and because at times cardiac lesions precede the first recorded attack of rheumatic fever. Some idea of the duration of the disease can, nevertheless, be obtained by assuming that the first recorded attack of rheumatic fever represents the time of onset of the infection. The error in such an assumption would make the average duration of the disease longer than that indicated by the clinical data to be presented. This error is counteracted, on the other hand, by the fact that in some instances the onset of cardiac damage may have been independent of the first attack of rheumatic fever.

The duration of rheumatic heart disease was studied in a group of patients with necropsies, in whom rheumatic heart disease was eventually the cause of death. An earlier analysis showed that of 369 patients with unquestionable rheumatic heart disease, 44 per cent died of this disease; in 11 per cent rheumatic heart disease was a contributing cause; in 17 per cent death was due essentially to subacute or acute bacterial endocarditis on a rheumatic basis; and in 27 per cent it was due to causes not associated with rheumatic heart disease. The data presented in this communication bear only on cases in which death was caused by rheumatic heart disease.

Age of Onset. The clinical data in 108 cases with necropsies clearly indicated whether or not there had been a previous rheumatic infection. Eighty-three of these cases, 40 males and 43 females, gave a definite history and 9 a suggestive history of either rheumatic fever

*From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School.

or chorea. In 16 cases there was no recollection of any previous rheumatic manifestation. Thirty additional cases were included with a definite history of rheumatic infection but without necropsy studies, making a total of 113 cases with positive rheumatic histories.

TABLE I

AGE OF ONSET OF FIRST ATTACK OF RHEUMATIC FEVER IN 113 CASES

AGE GROUP	CASES	
Years	*No.*	*Per Cent*
0-10	31	27.4
11-20	46	40.8
21-30	16	14.1
31-40	14	12.4
41-50	4	3.5
51-60	1	0.9
61-70	1	0.9
71-80	0	0.0

Table I shows the distribution according to age of onset of rheumatic fever or chorea. The earliest age of onset was three years; in 3 cases infection was acquired at five years. The majority of instances in the first decade, however, occurred nearer the age of ten years. In accordance with general knowledge, a high percentage was noted in the first and second decades, 77 patients having had their first attack before the twentieth year. A smaller but appreciable group apparently acquired the infection in the third and fourth decades, and 4 in the fifth decade. In one instance the first and fatal attack occurred in the sixty-first year, and gross and histological evidence of a typical acute rheumatic pancarditis was found on post-mortem examination.

Relation of First Attack to Onset of Cardiac Damage. Some opportunity to answer the question as to whether the first recorded attack of rheumatic fever was coincident with the earliest cardiac damage was presented in 10 cases in which a first attack of rheumatic fever resulted in a fatal attack of heart disease. In 5 of these 10 cases, valvular and myocardial lesions were entirely acute; there was no gross or microscopic evidence of a past infection as indicated by chronic inflammatory reactions. In the group showing evidence of old rheumatic heart disease the degree of involvement was slight in 3 patients and marked in 2. The ages of the 5 patients with acute lesions were 13, 22, 35, 35, and 61 years; the ages of those showing fresh as well as old lesions were 11, 15, 19, 22, and 35 years. The duration of illness in 8 of these 10 patients was one month or less; in 2, six and eight months.

In this group of 10 cases, then, the onset of the first recorded rheumatic infection corresponded with the onset of demonstrable rheumatic heart disease in but 50 per cent. Deductions as to the significance of the first recorded attack cannot be drawn from so small a group. It

is interesting, however, that onset of rheumatic carditis should so often—in 4 out of 5 cases—be associated with an attack of rheumatic fever occurring for the first time in adult life.

Duration of Life After First Attack. The duration of life after the first recorded attack of rheumatic fever in 83 fatal cases is shown in Table II. Twenty-five patients lived five years or less, 6 having died from the initial attack and 8 in less than two years from the time of onset. The remainder showed a duration of life ranging from six to

TABLE II

DURATION OF LIFE AFTER FIRST ATTACK IN 83 CASES WITH NECROPSY RECORDS

DURATION OF LIFE	CASES
Years	*No.*
0- 5	25
6-10	10
11-15	10
16-20	13
21-25	10
26-30	5
31-35	7
36-40	3

forty years after the earliest manifestation. As would be expected, rheumatic cardiac activity at death is more frequent in patients dying a short time after the first attack of rheumatic infection. In an unselected group of 21 patients in whom death occurred within three years after onset of infection, activity was noted in 18; in a second unselected group comprising 19 patients who had lived twenty-five or more years after the first infection, activity was noted in 9.

TABLE III

DURATION OF LIFE IN 36 CASES OF RHEUMATIC FEVER ACCORDING TO AGE AT ONSET OF FIRST ATTACK

18 CASES WITH ONSET BEFORE AGE OF 10	18 CASES WITH ONSET AFTER AGE OF 26
Years	*Years*
2	0
2	0
2	0
3	0
10	1
12	4
14	5
15	7
15	8
18	8
20	10
20	10
21	12
27	20
32	20
32	20
34	25
35	25

There is a general belief that rheumatic infection is more damaging to the myocardium in the early years of life than when it occurs for the first time after the age of twenty-five years. Table III gives the duration of life in two groups: one, in which the first attack occurred at or before the age of ten; the other, in which the first attack occurred at or after the age of twenty-six years. In the latter group the duration of life was appreciably shorter, and death followed soon after the first attack of rheumatic fever in 5 cases, whereas in the first group no immediate fatality occurred. The duration of life was approximately 30 per cent longer in Group 1. This finding suggests that the rheumatic infection is more damaging to the heart when the first attack occurs in an adult. Another possible explanation of the difference, however, may be that after adult years the first recorded attack of the rheumatic infection is less likely to represent the true onset.

DURATION OF HEART FAILURE

An analysis was made of the duration of the cardiac symptoms, as indicated by the duration of the "present illness" in 134 patients eventually dying as a result of rheumatic heart disease. The "present illness," as employed in this study, covers the period from the onset of *significant and progressive symptoms* to the time of death. In some instances in which the patients gave a history of having had symptoms for many years, the exact time of onset was not clear, either because of the insidious character of the progression, or because, as often happens, patients who are informed in early youth that they have heart disease go through life with a mild neurosis or fear of overexertion, and date the onset of symptoms from the time of the medical diagnosis. In other and rather frequent instances there is a true but slight limitation of the cardiac reserve which remains stationary for many years, after which a definite downhill progression of symptoms occurs. Eleven of the 134 cases studied for the duration of symptoms showed an initial period of several years in which there was either such mild limitation of circulatory efficiency or a neurosis manifesting itself as such. The preliminary period in these 11 cases was not regarded as a part of the present illness.

The character of onset and the course of cardiac manifestations showed wide variation. The following are characteristic clinical groups:

1. Acute Heart Failure and Rapid Death. The illness is of sudden onset with severe pulmonary symptoms in a patient previously in good health. The patient is forced to bed with marked dyspnea, orthopnea, cyanosis, pulmonary congestion and edema, and dies within from two days to six weeks.

2. Acute or Subacute Heart Failure With Recovery. There is a relatively sudden onset of weeks or months in duration, as in Group 1, but

recovery occurs. The recovery is either complete within a few weeks, with freedom from all symptoms, or partial, with persisting dyspnea on exertion and limitation of cardiac reserve. Prognosis is difficult, for death may occur at any time within from three months to ten years, and after one or more attacks of failure. It may occur as a climax to increasing limitation of reserve, or precipitately as acute failure.

3. Progressive Heart Failure. In this group the onset is gradual, with slowly progressive failure over a period of from one to three years. Recovery is slight or insignificant in spite of prolonged bed rest. The cardiac reserve steadily diminishes and death ensues.

4. Gradual Onset of Heart Failure With Recovery of Short Duration. The onset is as in Group 3 but with some recovery after prolonged rest and digitalis. There is relative comfort for a period of several months, but rarely longer; failure then occurs and death ensues.

TABLE IV

DURATION OF HEART FAILURE IN 134 FATAL CASES

DURATION OF FAILURE	CASES	
Months	*No.*	*Per Cent*
1 or less	36	27
6 or less	62	46
12 or less	78	58
Years		
1 or more	56	42
3 or more	44	33
5 or more	19	14
10 or more	5	4
15 or more	3	2

Table IV presents the distribution of the 134 cases according to the duration of "present illness." Twenty-two patients died within two weeks from the time of onset of definite cardiac symptoms; 36 within one month; 62 within six months; and 78, or more than 50 per cent, within one year. Forty-four cases showed a duration of illness of three or more years, 19 cases of five or more years, and 5 cases of ten or more years.

TABLE V

DURATION OF LIFE AFTER ONSET OF CONGESTIVE FAILURE IN 56 CASES WITH TOTAL ILLNESS EXCEEDING 1.5 YEARS

DURATION OF LIFE	CASES
Months	*No.*
1 or less	11
2- 6	14
7-12	4
Years	
1.5-3	16
3.5-5	6
6- 10	5

Duration of Congestive Failure. It is of prognostic importance to obtain information as to the expectancy of life after the onset of definite congestive failure necessitating rest in bed. Accordingly, the duration of life in this stage of failure was analyzed in a group of 56 cases with a total duration of illness, including the period preceding the congestive failure, of one and one-half years or longer (Table V). In some of these cases there were one or more intervals of relative improvement after the onset of severe failure. In 27 cases, or approximately one-half, congestive failure persisted for more than one and one-half years. In 11 cases, death occurred after failure had been present one month or less.

Factors Determining an Acute Fulminating Course. One of the striking findings among these patients with rheumatic heart disease was the high frequency of acute cardiac deaths. Some of the factors which may be responsible for such a fulminating course are: active rheumatic infection, infections other than rheumatic, embolism, and pulmonary complications, including sudden general or left-sided failure with pulmonary edema. *Sex* apparently is not a significant factor, since in a group with an illness lasting six months or less there were 33 males and 31 females, and in a group with an illness of two years or more, 23 males and 32 females. *Age*, likewise, does not appear to be a related factor. A correlation of the clinical course with the postmortem findings, on the other hand, suggests that the presence of *activity*, and particularly the site and degree of the activity, is of importance. Thus, in a group of 36 patients with an illness of one month or less, activity was present in 26. In a group of 29 patients with an illness of four years or longer, there was activity in 5, questionable activity in 5, and absence of active infection in 19. A comparison of these groups suggests that active carditis, if sufficiently severe, may precipitate a rapid downhill course.

In some patients *embolism* obviously resulted in a rapid course. Embolism usually occurs in the presence of auricular fibrillation, early

TABLE VI

CAUSE OF DEATH IN 36 CASES WITH A CARDIAC ILLNESS OF ONE MONTH OR LESS IN DURATION

CAUSE OF DEATH	NO. OF CASES
Embolism	8
Failure with active carditis	8
Failure without active carditis	5
Failure with active carditis and terminal infection	4
Failure with active carditis and pulmonary atelectasis	3
Failure without active carditis and with terminal infection	2
Failure with active carditis and acute nephritis	2
Failure with pregnancy	1
Failure with embolism and infection	1
Purulent pericarditis	1
Unknown	1

or late in the course of congestive failure.[3] Thus in the group of 36 patients with an illness of one month or less, significant embolism occurred eight times, as compared with seven times in a group of the same size with an illness of four years or longer.

Table VI shows the clinical state just before death in 36 patients with a fulminating course. Embolism was responsible for death in 8 patients. General failure was present in 26, and in 17 of this number active carditis was found. In 7 of the 17 with active carditis, terminal infection, usually bronchopneumonia, occurred. In 3 patients with general failure and carditis, significant pulmonary atelectasis was found at the post-mortem examination. In 5 patients the final failure was unaccompanied by infection. In 1 patient general failure was apparently precipitated by the terminal months of pregnancy. In 2 patients general failure with active carditis and acute nephritis coexisted. The exact rôle of the acute nephritis in the causation of death was difficult to evaluate.

An analysis of the *degree of valvular damage* in the same 36 patients showed moderate valvulitis with stenosis of either mitral or aortic valves in 14 patients and marked changes in 2. The remaining patients showed only minor lesions of the valves, stenosis being only slight or absent in most instances. The death of patients not dying of such complications as embolism was, therefore, in all probability due to myocardial damage. The condition of the myocardium in 17 patients may have been significantly aggravated by the active rheumatic infection. In the 2 patients with marked valvular lesions there was no evidence of active infection, and it is probable that death was due chiefly to mechanical failure.

DISCUSSION

This study, as well as the data presented in previous communications,[1, 2] confirms the common clinical observation that the course of rheumatic heart disease shows great variation. In the entire group of 474 cases there were 269 in which death was due to causes other than rheumatic heart disease.[1] In these cases, as well as in those in which cardiac damage was only partially responsible for death, it was not feasible to study the life history of the disease. The clinical course of rheumatic heart disease, as observed in the cases here analyzed, is that characteristic of cases in which cardiac damage eventually leads to death; hence the data presented are not comparable with those obtained from the study of patients irrespective of the degree of cardiac involvement.[4, 5]

The distribution of cases in the present group according to the age at onset of rheumatic infection corresponded closely with that in the group observed clinically by Willius.[6] Analysis according to duration of life after onset of rheumatic fever showed an approximately equal

distribution in the group less than two years, the group two to five years, and in the five-year periods up to twenty-five years. A smaller number of patients lived as long as forty years after the first infection, ultimately succumbing to the heart disease. Since duration of life varies so greatly, one cannot speak with justification of the average duration of life after the first infection. Prognostication as to expectancy of life after the first infection is, therefore, not feasible. In accordance with the findings of Willius,[6] there is some tendency toward a shorter duration of life when the first infection develops after the age of twenty-five years than when this occurs before the age of ten years. This difference cannot be explained by the shorter expectancy of life after the age of twenty-five years. A probable interpretation is that adults are less tolerant to rheumatic cardiac infections.

The fact that in many cases the duration of life is short following the appearance of cardiac symptoms, and particularly following the onset of congestive failure, is significant. Thus, of the patients presenting these symptoms, 58 per cent were dead within a year after the onset of cardiac symptoms. As high as 27 per cent exhibited cardiac symptoms or signs of less than one month's duration. Age and sex, as well as the distribution and the degree of valvular damage, played no significant rôle in the precipitation of this rather acute type of cardiac death. Acute rheumatic myocarditis, embolism, and acute infections other than rheumatic fever were the most frequent precipitating factors. Laws and Levine[7] have also emphasized the frequency of death resulting from causes other than chronic failure of the myocardium.

SUMMARY

1. Data are presented bearing on the course of fatal rheumatic heart disease as obtained from the records on 113 cases and 83 necropsy examinations.

2. The age at onset of the first rheumatic infection varied from three to sixty-one years, the majority of cases occurring in the first and second decades.

3. The duration of life after the onset of clinical evidence of rheumatic infection varied from a few weeks to forty years. About 50 per cent of the patients lived from six to twenty-five years, the number of cases showing fairly even distribution according to five-year intervals.

4. More than 50 per cent of the patients died within one year after the onset of definite cardiac failure.

5. The clinical types of heart failure encountered are described, and the high frequency of relatively short duration of life following the onset of significant cardiac symptoms, and particularly of congestive

failure, is analyzed. Almost one-third of the patients succumbed as a result of a fulminating course precipitated by factors other than chronic myocardial failure.

6. In the fulminating fatal course acute carditis, embolism, and infections other than rheumatic fever played the most significant rôles.

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THE TWO-STEP TEST OF MYOCARDIAL FUNCTION*

ARTHUR M. MASTER, M.D.
NEW YORK, N. Y.

FOR many years, tests of myocardial function have been a common procedure in physiological and medical institutions and also in the office of the medical practitioner. The large number of reports and the variety of methods described, however, suggest that a satisfactory routine test has not been found. The tests in the main are not for quantitative measurement, and the few that are measurable have no standards for normal individuals in relation to sex, age, and weight. Another important criticism is that many methods utilize unusual muscular movements.

As early as 1889, and between then and 1904, observations[1-4] were reported showing that systolic blood pressure and heart rate rose during and directly after muscular work and declined later. In the following review of the tests described in the literature and in my own test, blood pressure and pulse rate readings made after a certain interval of time subsequent to a definite exertion are compared with the resting blood pressure and pulse rate figures before the exertion. If these two readings are practically the same, the individual is considered to have a good, or normal, myocardial function.

The form of functional test of the heart is usually some body movement, such as flexing and extending the arm, flexing the trunk, or knee-bending.[5-9] Kahn[10] introduced hopping on each foot 100 times, and all kinds of modifications of this test are in common use. For instance, the patient may be asked to hop twenty, forty or more times on each foot.

Stair climbing was in vogue for many years and is somewhat used at the present time. Selig,[11] as early as 1905, was an exponent of this form of test. Rapport[12] directed his patients to mount 45 and 90 steps, each 9 inches high. These climbs were made at different speeds. Wilson[13] employed 25 and 60 steps. Although this worker made quantitative measurements, sex, age, weight and height were not taken into consideration. Magnus-Alsleben[8] and Felberbaum and Finesilver[14] also used stairs or steps—the latter built two steps each 6 inches high.

In 1901, Brittingham and White[15] used dumb-bell swinging, from floor to an arm's length overhead. Barringer,[16-19] in a series of articles published between 1915 and 1922, popularized this type of test, and

*From the Cornell Clinic and the Department of Medicine, Cornell University Medical College, New York, N. Y.

Mann[20] applied it to the study of patients during convalescence. Cotton, Rapport and Lewis[21] considered the total work done. Barringer[18] demonstrated that work performed with the arm and back muscles gave the same results as work with the thighs and legs. Wilson[13] reported that the results of stair climbing and rope jumping were similar to those of dumb-bell exercise. Barringer[17] stated that the outcome varied but slightly from day to day in the same individual. It will be shown that this was found to be true, also, when the test described in this paper was used. This uniformity enhances the value of a test. In 1922, Barringer[19] suggested that normal standards of exercise tolerance for adults should be worked out.

For essentially quantitative tests, one must refer to the stationary bicycle, visible but now seldom used in the physiology department of a medical school. Ergostats and ergometers, where the muscles of the fingers, arm or leg come into play, have been described by Mendelsohn,[22] Gräupner,[23] Benedict and Carpenter,[24] Krogh,[25] Cathcart, Wishart and McCall,[26] and Gillespie, Gibson and Murray.[27]

A criticism of the prevailing tests, as already stated, is that they either do not measure work performed quantitatively, or that the same exertion is required of male or female, young or old, light or heavy individual. Of equal moment is the criticism that no standards for normal individuals have been constructed.

In 1929, E. T. Oppenheimer and I[28] published an account of a "two-step" test which supplied a quantitative measurement of work. In performing this test, only ordinary everyday muscular activity is called into play, the procedure is a definite and simple one, and it may be carried out in a physician's office or in a clinic.

The subject of functional tests is reviewed for two reasons. (1) New tables* (Tables I and II) have been constructed which immediately give the required number of ascents for a given weight and age without further arithmetical calculation, and all interpolations and corrections for age and height have been obviated. (2) The later tables are based on the results of approximately 1,500 tests carried out upon

*Dr. P. V. Wells, the biophysicist of the Prudential Life Insurance Co. of America, calculated the mathematical graduations necessary for the construction of these tables.

The experimental material upon which the revised tables are based resulted from the testing of 210 males and 234 females, four to seventy-four years of age. The maximum number of ascents performed without delaying the return of the blood pressure and pulse rate to normal was recorded. From this data and the patient's weight the work performed in foot pounds per minute was calculated. The work done is recorded in terms of climbs, this being considered a better estimate of physical fitness than foot pounds, as it measures the relative efficiency of subjects in handling their weight, as it affects the circulation.

The original tables were based on partial correlation equations in terms of sex, age, and weight, but the inconsistencies in the coefficients indicated that the correlation with height was a spurious effect of the relation between height and weight.

Statistically, the process of "smoothed medians" was used. In the graduation each median was "weighted" by the actual number of cases in its age and weight class. The table of median ascents showed clearly that children of median weight accomplished over 30 ascents, while adult males of median weight did not exceed 25, and adult females reached only 23 ascents. For a given age, the numbers decreased steadily with increasing weight.

TABLE I

STANDARD NUMBER OF ASCENTS FOR MALES

WEIGHT (LB.)	AGE IN YEARS												
	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69
40- 49	35	36											
50- 59	33	35	32										
60- 69	31	33	31										
70- 79	28	32	30										
80- 89	26	30	29	29	29	28	27	27	26	25	25	24	23
90- 99	24	29	28	28	28	27	27	26	25	25	24	23	22
100-109	22	27	27	28	28	27	26	25	25	24	23	22	22
110-119	20	26	26	27	27	26	25	25	24	23	23	22	21
120-129	18	24	25	26	27	26	25	24	23	23	22	21	20
130-139	16	23	24	25	26	25	24	23	23	22	21	20	20
140-149		21	23	24	25	24	24	23	22	21	20	20	19
150-159		20	22	24	25	24	23	22	21	20	20	19	18
160-169		18	21	23	24	23	22	22	21	20	19	18	18
170-179			20	22	23	23	22	21	20	19	18	18	17
180-189			19	21	23	22	21	20	19	19	18	17	16
190-199			18	20	22	21	21	20	19	18	17	16	15
200-209				19	21	21	20	19	18	17	16	16	15
210-219				18	21	20	19	18	17	17	16	15	14
220-229				17	20	20	19	18	17	16	15	14	13

Table II

Standard Number of Ascents for Females

Weight (lb.)	Age in years												
	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69
40- 49	35	35	33										
50- 59	33	33	32										
60- 69	31	32	30										
70- 79	28	30	29										
80- 89	26	28	28	28	28	27	26	24	23	22	21	21	20
90- 99	24	27	26	27	27	26	25	24	23	22	21	20	19
100-109	22	25	25	26	26	25	24	23	22	21	20	19	18
110-119	20	23	23	25	25	24	23	22	21	20	19	18	18
120-129	18	22	22	24	24	23	22	21	20	19	19	18	17
130-139	16	20	20	23	23	22	21	20	19	19	18	17	16
140-149		18	19	22	22	21	20	19	19	18	17	16	16
150-159		17	17	21	20	20	19	19	18	17	16	16	15
160-169		15	16	20	19	19	18	18	17	16	16	15	14
170-179		13	14	19	18	18	17	17	16	16	15	14	13
180-189			13	18	17	17	17	16	16	15	14	14	13
190-199			12	17	16	16	16	15	15	14	13	13	12
200-209				16	15	15	15	14	14	13	13	12	11
210-219				15	14	14	14	13	13	13	12	11	11
220-229				14	13	13	13	13	12	12	11	11	10

444 normal persons, male and female, whereas the previously published tables were derived from a much smaller group of about 500 tests of 115 normal individuals. The tests were practically all performed at the Cornell Clinic of the Cornell University Medical College between the years 1927 and 1933.

METHOD OF PERFORMING THE TEST

The contrivance employed in this method of testing the functional condition of the heart consists of two steps,* each 9 inches high, so that one climb is one and one-half feet above the ground. (Fig. 1.) The number of ascents which the individual

Fig. 1.—Two steps, each accurately 9 inches high, are placed near a wall or table. One climb is an ascent and descent. The patient always turns toward the wall before re-commencing another ascent.

should, theoretically, perform is obtained from the tables, and is determined by the patient's age and weight. The resting blood pressure and pulse rate are taken in the sitting or lying posture and are usually obtained within three to five minutes. Readings of the blood pressure and pulse rate are repeated until two in succession are practically the same. The patient then walks up one side of the steps and down the other, always turning toward the same side of the room or table before each ascent. This necessitates a change of direction at each turn and thus giddiness with its resulting artificial changes in the blood pressure and pulse rate is prevented.

*These steps can easily be built at home or office. Dr. L. F. MacKenzie has designed a compact folding pair of steps which Becton, Dickinson & Co., of Rutherford, N. J., have placed on the market.

In a minute and a half the patient makes his required number of ascents and then sits down. Two minutes after cessation of exercise the blood pressure and pulse rate should have returned to resting figures. Ten points difference in the blood pressure or pulse rate is the extreme limit permitted.

A definite example will be given. The work capacity of a man forty-four years of age, weighing 150 pounds, was required. In the tables, the vertical column of figures under forty-four years of age and the horizontal row opposite 150 pounds intersect at 22. This is the number of climbs or amount of work, so measured, that a normal man of this patient's age and weight should be able to perform. The blood pressure and pulse rate readings were these:

BLOOD PRESSURE	PULSE RATE
118/80	66
112/78	60
110/76	60

Obviously, the last readings were the patient's resting figures. He was started on his 22 climbs, and his rate was regulated so that he should perform exactly this number in one and one-half minutes. He then sat down again. At the end of two minutes, the readings were: blood pressure 116/78 and pulse rate 62 beats per minute, which are within the ten point difference allowed. In other words, the patient's exercise capacity was normal. The work performed was: 22 climbs × 150 lb. weight × 1½ feet height = 4,850 ft. lb. This work, however, was done in 1½ minutes. Per unit of time, that is, per minute the work was: $\frac{22 \times 150 \times 1\frac{1}{2}}{1\frac{1}{2}}$ or 22 × 150 = 3,300 ft. lb. Hence, merely the weight in pounds multiplied by the number of climbs gives the work per minute.

Not only may one ascertain in this way whether an adult or child is fit to perform the average physical work for his sex, age, and weight, but one can learn, also, what is his actual physical capacity, be he invalid or athlete. The number of climbs that the subject is able to perform divided by the number he should be able to perform, according to the table, gives his percentage of efficiency. A few illustrative cases will make this clear.

CASE 1.—Mrs. A. R., aged fifty-three years, weight 156 pounds. Her diagnosis was chronic rheumatic valvular disease, mitral stenosis and insufficiency, an enlarged heart. The theoretical average number of ascents, for her age and weight, obtained from the table, is 17; but two tests were performed on May 22, 1931, the first of 14 ascents, and the second of 12. The resting figures were: blood pressure 130/96, heart rate 82 beats per minute. Two minutes after 14 ascents: blood pressure 140/96, heart rate 96 beats per minute. It is obvious that 14 climbs was too much, as the heart rate difference was fourteen whereas the extreme limit is ten. Later in the day, twelve climbs were essayed. The resting readings were: Blood pressure 150/100, heart rate 96 beats per minute. Two minutes after 12 ascents: blood pressure 146/96, heart rate 96 beats per minute. This last test was well performed, and hence her limit was between 12 and 14, that is, 13. In foot pounds this would be 13 × 156 = 2,028 ft. lb. In percentage of efficiency $\frac{13}{17}$, or 77 per cent.

The two-step test occasionally has given us evidence revealed by no other means at our disposal. The following case history is that of a man with a bad myocardium in whom for a long time the exercise tolerance was the only abnormal finding.

CASE 2.—MR. R. P., aged fifty-two years, weight 149 pounds, sustained an acute coronary artery occlusion while in Miami, Florida, April, 1932. He had had an essential hypertension. I first saw the patient on June 30, 1932, and have followed

his case to the present time. The electrocardiogram, which during the April occlusion had revealed inversion of T_1, on July 6, 1932 (Fig. 2*A*), disclosed slight R-T abnormalities. The patient did not complain, the physical examination was negative, and according to the x-ray film the heart and aorta were normal. The exercise tolerance test, however, showed only 14, whereas the normal for one of his weight and age is 21. His percentage of efficiency was, therefore, $\frac{14}{21}$ or 67 per cent. Because of this low exercise tolerance he was given a guarded prognosis and classed as totally disabled at the time. Although he retired from business and retained a trained nurse, he did not improve and suffered another acute coronary artery occlusion on July 8, 1933, from which he has only barely recovered.

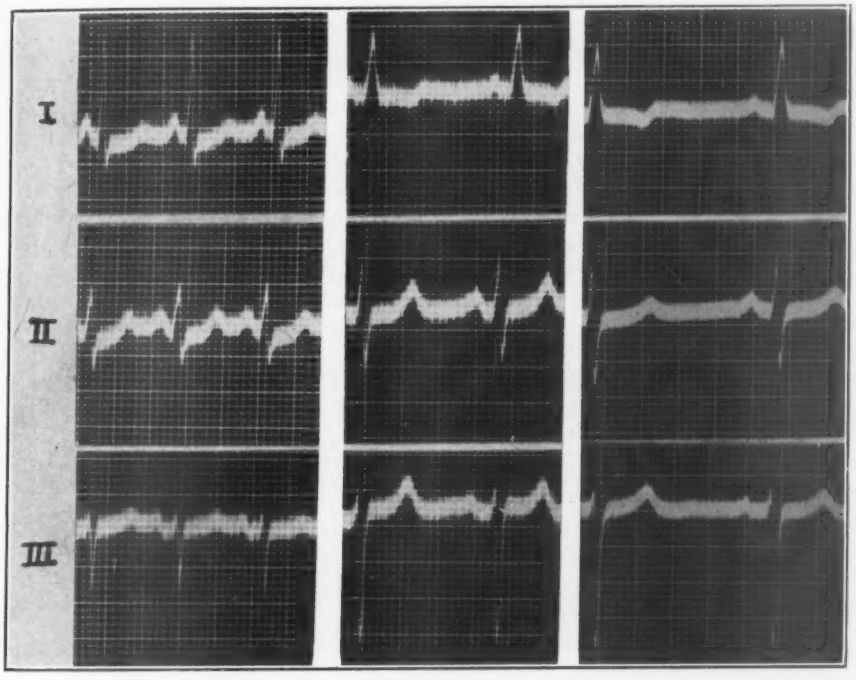

Fig. 2.—*A*, Case 2, Patient R. P., fifty-two years old. Although the electrocardiogram July 6, 1932, revealed only slight RS-T abnormalities, the exercise tolerance was poor and the percentage of efficiency was only 67. The patient developed an acute coronary artery occlusion July 8, 1933.

B and *C*, Case 3, Patient B. M., fifty-two years old. *B*, Electrocardiogram, June 22, 1931, disclosed definite T-wave inversion in Lead I, but the exercise tolerance was fairly good and the percentage of efficiency 86.

C, Electrocardiogram, February 15, 1934, the same. Exercise tolerance improved, percentage of efficiency 95. Patient still well.

Following is the story of a patient whose exercise tolerance test gave a truer picture of his cardiac condition than did his definitely abnormal electrocardiogram and one which the history of his case would not lead one to suspect.

CASE 3.—Mr. B. M., also fifty-two years old, was first observed by me on April 7, 1931, a few months after he was said to have had an acute coronary artery occlusion. He had weighed 230 pounds before this episode, but his weight at the time of observation was 179 pounds. The patient was taking digitalis and was working. Although he was advised to discontinue the digitalis and to stop work, he did neither. April

14, 1931, he sustained another severe acute coronary artery occlusion. For twelve weeks he was in bed, very ill. His diet was kept at a minimum so that when he was permitted out of bed he weighed only 150 pounds. His electrocardiogram, March, 1932, (Fig. 2*B*) showed the T-wave in Lead I to be definitely inverted and the QRS waves to be slurred. The patient's exercise tolerance on that date was 18, which was fairly good; efficiency was $\frac{18}{21}$ or 86 per cent. His prognosis was, therefore, considered good. Although the electrocardiographic picture has remained absolutely unchanged to date (Fig. 2*C*), his exercise tolerance has improved. By December, 1932, it was: $20 \times 150 = 3{,}000$ ft. lb. or $\frac{20}{21} = 95$ per cent efficiency. Because of this good exercise tolerance and despite the same definitely abnormal indications of the electrocardiogram, the patient was permitted to return to his regular work, as a sugar broker. For the last fourteen months he has worked as hard as he did before he became ill, has had no complaint and looks better than he ever did. The exercise tolerance in February, 1934, was absolutely normal, that is, 21 ascents.

One of the most difficult questions to answer is that of a patient when he asks, "How much work may I do?" The exercise tolerance test is of distinct aid in making a wise reply. The test is an objective method and serves to distinguish the neurasthenic or malingerer from the truly incapacitated.

It has been suggested that a patient's work capacity probably varies from day to day, but those using the test have been impressed with the uniformity of the number of ascents for an individual. Thus, if one's limit is 25 climbs today, it will be that tomorrow and probably weeks and months later, provided the weight remains approximately unchanged. If he tries 26 climbs, he will fail to do this. Examples will demonstrate these principles.

On November 14, 1926, the "two-step" test was performed by a man thirty-one years of age, weighing 157 pounds and 5 ft. 10 in. in height. This person was then in exceptionally fine physical condition as a result of handball playing, swimming in indoor pools, etc. It is not surprising, then, that he was able to perform an unusual number of climbs, namely 33.

	TIME	BLOOD PRESSURE	PULSE
Final resting figures		120/76	62
Exercise started	11:57:00 A.M.		
Exercise ended (33 climbs)	11:58:30		
	11:59:00	200/78	118
	11:59:35	140/78	76
	11:59:55	136/76	72
Two minutes after exercise	12:00:30	124/78	64

Although this man was much more dyspneic than the average individual who performs less climbs, his blood pressure and pulse rate returned to within ten points of resting figures.

Nearly eight years later, May 17, 1934, the test was repeated on the same man who was now thirty-nine years of age and weighed 162 pounds.

	BLOOD PRESSURE	PULSE
	126/86	76
	118/86	72
	118/84	68
Resting figures	118/84	68
Two minutes after 26 climbs	132/84	68

It is evident that 26 climbs exceeded the man's limit, as the difference between the resting systolic blood pressure and that two minutes after exercise was more than ten. On June 5, 1934, the test was again performed.

	BLOOD PRESSURE	PULSE
	110/82	80
	108/84	80
Resting figures	108/82	80
Two minutes after 25 climbs	118/78	80

It was, therefore, concluded that this man could perform 25 climbs and no more. This conclusion was borne out by further observations on June 6, 1934, at 9:50 A.M. as follows:

	BLOOD PRESSURE	PULSE
	114/78	76
	114/76	72
Resting figures	112/76	72
Two minutes after 26 climbs	126/78	80

Again 26 had been too much. The test, repeated at 12:18 P.M., disclosed, as usual, that 25 could be performed.

	BLOOD PRESSURE	PULSE
	114/84	64
	114/82	68
	112/80	68
Resting figures	112/80	68
Two minutes after 25 climbs	118/78	68

It has been mentioned already that Barringer[18] observed that his results varied only slightly from day to day in the same individual. The present observations corroborate his conclusion. This invariability makes the two-step test dependable.

COMMENT

Not only does clinical experience seem to demonstrate that the two-step test is a measure of myocardial capacity, but when one turns to the mathematical formulas, established by the physiologists, for the work performed by the heart, one observes that this work is directly related to the mean arterial pressure and the pulse rate which have been used as factors in the present test. In 1895, Frank[29] published the formula $A = P V + (\frac{1}{2} mv^2)$, in whch A represents the work of the heart, P, the mean arterial pressure of the aorta, and V, the volume of blood ejected at each heartbeat, (m = the mass of ejected blood, and v = its velocity). The mean arterial pressure of the aorta is related directly to the systolic and diastolic blood pressure, and the work per minute is, therefore, the work per cardiac contraction multiplied by the pulse rate. Evans and Matsuoka,[30] Tigerstedt,[31] and Wiggers[32] have used the same formulas as Frank; the first half of the equation representing the work of the heart in overcoming arterial resistance and the second, the kinetic energy imparted to the blood to move it along. The former, $P V$, in which the blood pressure appears is considered to be 90 to 99 per cent of the work of the heart in human beings. This appreciation that the work of the heart per minute is a function of the systolic and diastolic blood pressures and the pulse rate has led Barach[33] to use these three figures as an "index" of the functional capacity of the heart. He cited the formula S. D. R. in which the systolic and diastolic blood pressures were added and then

multiplied by the rate of the heart. This formula, of course, did not give the quantitative measurement of the work of the heart, and here the criticism applied to previous tests again is pertinent, namely, that no standard measurements have been constructed for normal people. The study of these formulas, nevertheless, proves that when considering the factors of blood pressure and heart rate one is concerned with figures directly related to the work of the heart. In the present test all three of these factors are utilized. Hence, for these reasons and from clinical experience, it is thought that the two-step exercise is a measure of "myocardial function."

The influence of a man's occupation and physical training has been noted. Whether a man be a sedentary worker, such as a bookkeeper, or an outdoor salesman, the number of climbs is in the usual normal range. In the case, however, of a man in strenuous physical training, such as a student on the football squad, it will be found that his limit is beyond the figures given in the table.

In the "two-step" test the systolic and diastolic blood pressures, measured by the auscultatory method, and the pulse rate have all been used. Each of these, two minutes after completion of the exercise, must return to within ten points of the resting figures. It has been observed in patients in whom this does not occur that it is usually the systolic blood pressure that does not return to "basal" figures. The pulse rate is next in frequency of nonreturn, and the diastolic blood pressure is found to vary least. Schellong[34] obtained similar results. This feature was brought out in the first test of the man whose exercise tolerance was reviewed eight years later. It would appear that when work is demanded of the heart the systolic blood pressure is first altered, then the pulse rate, and last the diastolic pressure. These statements have more than mere academic or even physiological interest, for they mean that the number of climbs accomplished do not "strain" the heart even temporarily. If normal persons are asked to perform many more climbs than are called for in the tables, there will be a delay of three, four, five, or six minutes before the readings return to resting levels. This has been shown by the many authors referred to earlier in the paper.

After considerable experimentation, a short duration of exercise, such as one and one-half minutes, had been found most useful. The same numeral, one and one-half, for the height of the steps simplifies the mathematical process in calculating the foot pounds of work performed. This has already been demonstrated in the present text, but these matters were more fully discussed in the article published in 1929.[28] An extensive experience seems to prove the advisability of this short and nonstrenuous form of exercise since no untoward accidents have ever occurred. In more than 100 cases of anginal syndrome

we have never observed a single onset of pain. Undoubtedly, had the rate of climb been accelerated or the duration of climb been increased, pain would have been elicited. In the average patient observed in office or clinic the test produces only slight fatigue and but moderate dyspnea. In fact, most patients have an inclination to perform more climbs than the number required. The two-step climbing test, therefore, meets all the requirements laid down by White[35] when he said, "A simple test is less apt to strain unaccustomed muscles of the subject, less apt to exhaust prematurely a person not in good physical

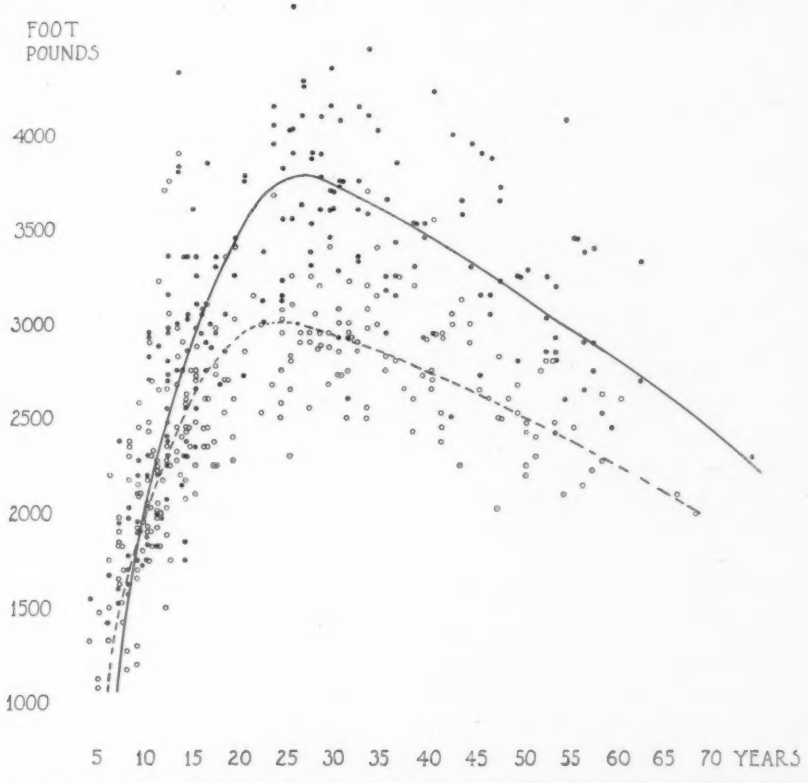

Fig. 3.—Relation of age to exercise tolerance as expressed in foot pounds of work per minute. Straight line (through dots) for male and broken line (through circles) for female individuals.

training and more convenient and practical to execute. In fact, such simple exertion as enters into the routine daily life of the patient is best of all."

The number of ascents itself is an index of physical efficiency and a consideration of "percentage" of efficiency is not essential, for foot pounds of work per minute, as has already been shown, is the number of climbs multiplied by the patient's weight. However, per unit of weight, that is per pound of the patient, this number would be divided

by the patient's weight, the result again being the number of ascents. Hence a patient's efficiency can be judged directly by his limit in climbs.

Up to the age of ten or eleven years, both boys and girls show a very rapid increase in number of foot pounds of work per minute. (Fig. 3.) There is a slowing down of this rapid ascent in females and the maximum of about 3,000 ft. lb. is reached between the ages of twenty and twenty-seven years. In men, however, a rapidly increasing capacity for work continues practically unabated until the age of twenty-two years, and between twenty-two and thirty-one years

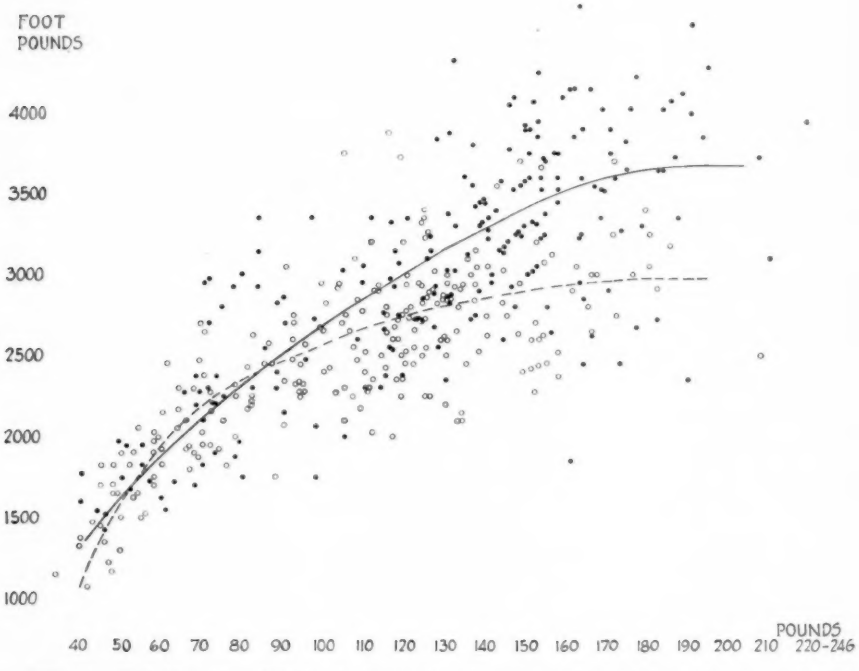

Fig. 4.—Relation of weight to foot pounds of work performed per minute. Straight line for male and broken line for female individuals.

the maximum of about 3,800 ft. lb. is reached. With advancing age, in both sexes, there is a steady, progressive decline in work capacity.

In general, the foot pounds of work performed increase rapidly with greater weight, until seventy to ninety pounds is reached. (Fig. 4.) The slope then becomes more gradual in the case of women. In men the slope is hardly changed, the maximum work is most often attained when men weigh 170 to 200 pounds and when women weigh 150 to 180 pounds. Men are capable of performing more work per weight, the maximum for men being about 3,700 ft. lb. of work per minute, for women about 3,000 ft. lb. of work per minute.

The test offers an unusual means of research. By it, one can classify quantitatively the myocardial reserve of patients with valvular disease. How do patients with mitral and those with aortic lesions compare? Does the exercise tolerance correspond to the heart size rather than to the valvular lesion? What are the quantitative limits of patients with an anginal syndrome, essential hypertension, exophthalmic goiter? Recovery from acute disease may be investigated. Occasionally, patients have complaints for as long as three to six months after an acute lobar pneumonia, of dyspnea on slightest exertion, fatigability, weakness, or rapid pulse, and in them the exercise tolerance has been found below normal. Simultaneously, with increase in work capacity, as indicated by the two-step test, the symptoms have disappeared. Frequently in a patient with an anginal syndrome the exercise tolerance has been the only objective evidence of myocardial impairment. In the malingerer it is normal.

It has been pointed out to me that the number and extent of the respiratory excursions are not considered in this test. This is a just criticism, but as three factors already are considered, namely, systolic blood pressure, diastolic blood pressure and pulse rate, it has seemed best not to complicate it by the addition of a fourth variable.

Precautions to Be Observed Before Test Is Performed.—A question that must and does arise is that of the lability and variability of the blood pressure and pulse rate. As excitement, emotion, and apprehension affect them, naturally, correct readings cannot be obtained when these influences are at play. I always find some means of having the patient rest comfortably, at least for five minutes, before blood pressure and pulse rate are recorded. Readings are repeated until the lowest is ascertained. It will be found that a basal or resting blood pressure and pulse rate exist in individuals just as there is a basal metabolic rate. It seems to make no difference whether the "resting" readings are taken in the sitting or in the lying position, provided the patient returns to the same position after the exercise.

Before the patient begins the ascents, the examiner demonstrates how the test is performed. The patient is assured that he is not to run, that he may gain support, or reassurance, by lightly placing one hand against the wall, and, in fact, the examiner may gently support the moderately sick patient by taking hold of one arm lightly, as the patient climbs the steps. As long as he is not given a vertical lift, this support does not interfere with the work which he performs.

There are other precautions which are important. Certain drugs lower the exercise tolerance. This applies to an individual who is receiving thyroid extract, or ephedrine, or who is taking alcoholic intoxicants or smoking excessively. Even one or two cigarettes smoked immediately before the test will have this effect. An acute upper respiratory infection, like a coryza, pharyngitis, tracheitis, sinusitis,

will show a similar lowering in limit of ascents. No special investigation of women during the menstrual cycle has been undertaken, but it has been observed that this affected the test in one woman. In two cases diagnosed as neurocirculatory asthenia the test showed the limit to be below average. In these people it may be, as White[36] has suggested, that the test is a measure of the "fitness of the nervous system" but this is a debatable question. It may be that in a person with effort syndrome the myocardial reserve is limited.

SUMMARY

A simple quantitative "two-step" test of myocardial function is described, and tables of climbs are given for normal individuals, from four to seventy-four years of age, of both sexes. The patient's weight multiplied by the number of ascents gives the foot pounds of work per minute. Not only may it be learned in this way whether the exercise tolerance of an individual is within average figures, but his actual limit may be ascertained. The percentage of efficiency is calculated by dividing the number of climbs the patient can actually perform by his theoretical limit, as derived from the tables.

Men have greater exercise tolerance than women. The maximum of this tolerance appears to be about 3,800 foot pounds of work, in men between twenty-two and thirty-one years of age weighing from 170 to 200 pounds. The maximum for women appears to be 3,000 foot pounds of work performed between the ages of twenty and twenty-seven by individuals whose weight is about 150 to 180 pounds. Older and heavier men and women show a decline in exercise tolerance. Children show the greatest efficiency, that is, the number of ascents possible in the given time is highest in the young. There is a sharp rise until puberty, then the slope is more gradual until the twenties are reached.

Thyroid extract, ephedrine, alcohol, excessive smoking, and upper respiratory infections affect the results.

The test is a definite aid in the diagnosis and evaluation of cardiovascular disease and in deciding how much work, or sport, or other activity the patient may be permitted. It also helps to differentiate functional and organic disease of the heart and is particularly useful in the anginal syndrome.

The measure of exercise tolerance determined by the two-step test is a fairly constant figure from day to day, and, unless one is in athletic training, similar results are common in those who lead a sedentary and those who live an outdoor life.

The exercise tolerance test may be the only objective evidence that the myocardium is involved.

The exercise test is not a strain, and no untoward results, even in cases of anginal syndrome, have ever been observed.

Clinical experience, mathematical deduction, and physiological reasoning appear to prove that the test is an index of myocardial function.

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THE CIRCULATORY RESPONSE TO EXERCISE IN PATIENTS WITH ANGINA PECTORIS*†

Therapeutic Implications

S. H. Proger, M.D., W. R. Minnich, M.D., and H. Magendantz, M.D.
Boston, Mass.

STUDIES of the pathological and clinical findings in patients with angina pectoris, begun by Jenner[1] in Heberden's time and continued to the present, have yet to establish a constant or predictable relationship, except in the instance of coronary thrombosis, between what is observed clinically and what is found on post-mortem examination. Coronary sclerosis is believed to be quite intimately connected with angina pectoris. It is well known, however, that sometimes even the most advanced cases of coronary arteriosclerosis are associated with no clinical phenomena whatever. Mönckeberg's[2] studies of the coronary arteries in the fatalities in the Great War showed that in 652 autopsies coronary arteriosclerosis was found in 353; similar observations were made by Rössle.[3] One is therefore tempted to conclude, as does the pathologist Aschoff[4] in remarking on the fact that angina pectoris has been observed where no coronary sclerosis was present, "that purely functional factors may be responsible for the genesis of the disease." Such inconsistencies between pathological and clinical observations would make it appear that perhaps the important differences between patients with angina pectoris and individuals in the same age group with no clinical evidence of heart disease might be more manifestly physiological than pathological.

Since angina pectoris is characterized by the development of pain on exertion, we have attempted to determine what happens during exertion in patients who suffer from angina pectoris which differs from what is known to occur in those who do not have angina pectoris. We refer, of course, to the so-called angina of effort. We have been unable to find any account of observations on patients with angina pectoris during exercise, although it is under such conditions that we should expect to find the chief differences between such patients and normal people. Wayne and Laplace[5] have recently recorded observations made immediately before and after attacks of angina pectoris induced by stair climbing. In this study the physiological events preceding and perhaps responsible for the attack were not observed. This was

*From the Medical Clinic of the Boston Dispensary, and the Department of Medicine, Tufts Medical School.

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TABLE I

DATA CONCERNING PATIENTS WITH ANGINA PECTORIS

PATIENT	AGE	SEX	HEIGHT	WEIGHT	BLOOD PRESSURE	DURATION	HEART SIZE	ELECTROCARDIOGRAM	REACTION TO EXERCISE*	COMMENT
L. N.	64	M	5′ 5″	154	160/90	2.5 yr.	Mod. enlarged	Left axis deviation	I	
B. A.	61	M	5′ 6″	171	120/90	2 yr.	Mod. enlarged	Left axis deviation	I	Thyroidectomy 10/28/33.
A. W.	68	F	5′ 3″	127	170/86	4 mo.	Normal	Left axis deviation with sharply inverted $T_{2, 3}$ and deep S_2	I	
I. S.	64	M	5′ 5″	175	106/75	2 yr.	Mod. enlarged	Inverted $T_{1, 2}$ with left axis deviation	I	Thyroidectomy 9/29/33. Probably coronary occlusion 10/13/33.
O. H.	68	M	5′ 4″	165	155/95	3 yr.	Mod. enlarged	P-R 0.21 sec. Inverted T_1. Low complexes	I	Thyroidectomy November, 1933.
T. C.	64	M	5′ 10″	169	160/90	1.5 yr.	Mod. enlarged	Left axis deviation	I	Thyroidectomy 11/22/33. Probably coronary occlusion Nov., 1932. Def. cor. occ. April, 1934.
C. E. C.	72	M	5′ 6″	155	118/73	3 yr.	Mod. enlarged		II	
L. K.	52	M	5′ 5″	170	170/110	2 yr.	Mod. enlarged	Left axis deviation with auricular extrasystoles	II	
E. L.	71	M	5′ 9″	188	170/100	5 yr.	Markedly enlarged	Left axis deviation $T_{1, 2, 3}$ erect. S_2 deep	II	Onset with probable cor. occlusion in 1929.
E. F.	60	M	5′ 8″	165	175/115	2 yr.	Normal	Normal axis with vent. extrasystoles	III	
P. W.	74	M	5′ 6″	145	160/90	14 yr.	Mod. enlarged	Left axis deviation. Inverted T	III	Probable coronary occlusion 1/3/33.
M. S.	44	M	5′ 6″	131	145/85	4 yr.	Normal	Left axis deviation. $T_{1, 2}$ inverted. Deep Q_3	III	
C. J. E.	63	M	6′	208	170/100	15 mo.	Mod. enlarged	Left axis deviation with low T_1. Erect $T_{2, 3}$	IV	
L. H.	67	M	5′ 7″	138	165/102	2 wk.	Mod. enlarged	Normal	IV	
J. C.	54	M	5′ 6″	166	150/84	2 yr.	Sl. enlarged	Normal	IV	
P. A.	43	M	5′ 4″	150	86/64	1 yr.	Normal	Left axis deviation. Coronary T_1	V	Onset with coronary occlusion Jan., 1932.
L. G.	52	M	5′ 3″	165	138/84	2 mo.	Normal	Left axis deviation. T-waves erect S_2 deep		

*Represents group classification referred to in the paper.

also true of the studies of Wood, Wolferth and Livezey[6] who observed electrocardiographic changes during attacks of angina pectoris; and of Bischoff.[7] Levine, Ernstene and Jacobson[8] noted changes occurring in pulse, blood pressure, and electrocardiogram before, during, and after induced attacks of angina pectoris; but these attacks were initiated by injections of adrenalin, and one cannot assume that the circulatory response to adrenalin corresponds to the response to effort. The mechanism of the induction of pain under the two circumstances may well be entirely different.

Seventeen patients with angina pectoris, sixteen male and one female, have been studied. Six normal subjects in the same age group served as controls. The ages ranged between forty-three and seventy-two years. In all patients the history was obtained of substernal pain brought on by exertion, relieved by rest. All patients were excluded where there was even the slightest doubt that they represented typical cases of angina of effort. The duration of angina pectoris in all cases, except two, was more than one year; in three patients there was a past history suggesting coronary thrombosis. Further pertinent data concerning the patients with angina pectoris are summarized in Table I.

METHOD

Observations were made at the same time of the day under the same conditions. Before exercise was begun, with the patient sitting quietly on a stationary bicycle, the blood pressure, pulse rate, respiratory rate, and respiratory minute volume were obtained. The patient then pedalled at a slow rate (fixed by metronome) and with a four-pound pull (185 kg. M. work per minute) for three minutes. During the exercise the number of heartbeats was recorded for each ten seconds. This was made possible through the use of a small portable cardiotachometer designed and constructed by V. Guillemin of Massachusetts Institute of Technology. Also, during exercise the blood pressure, respiratory rate, respiratory minute volume, and oxygen consumption were obtained for each minute. Immediately after exercise we continued to count the heartbeats in ten-second periods, and we recorded the blood pressure at intervals of one minute. Oxygen debt was measured for a ten-minute period. With such short and light exercise we found that at the end of ten minutes following the cessation of exercise the oxygen consumption had practically reached its pre-exercise level. Oxygen consumption was measured using the open circuit method, the air samples being analyzed in a standard Haldane apparatus.

To determine capacity for work without pain we allowed the patients to pedal at a fairly rapid rate and with a six-pound pull (395 kg. M. work per minute) until the first evidence of cardiac pain developed, at which point the exercise was stopped.

RESULTS

General.—There were four general types of response, the most striking disturbance in these groups being (1) failure of pulse rate to rise normally during exercise; this was accompanied by normal respiratory response; (2) the development of cardiac irregularity (extrasystoles) shortly before the onset of pain and its disappearance shortly after the cessation of exercise (the response of the cardiac rate, blood pressure and respiration was normal in these cases); (3) a thin, rapid, barely palpable pulse during exercise which became full and strong

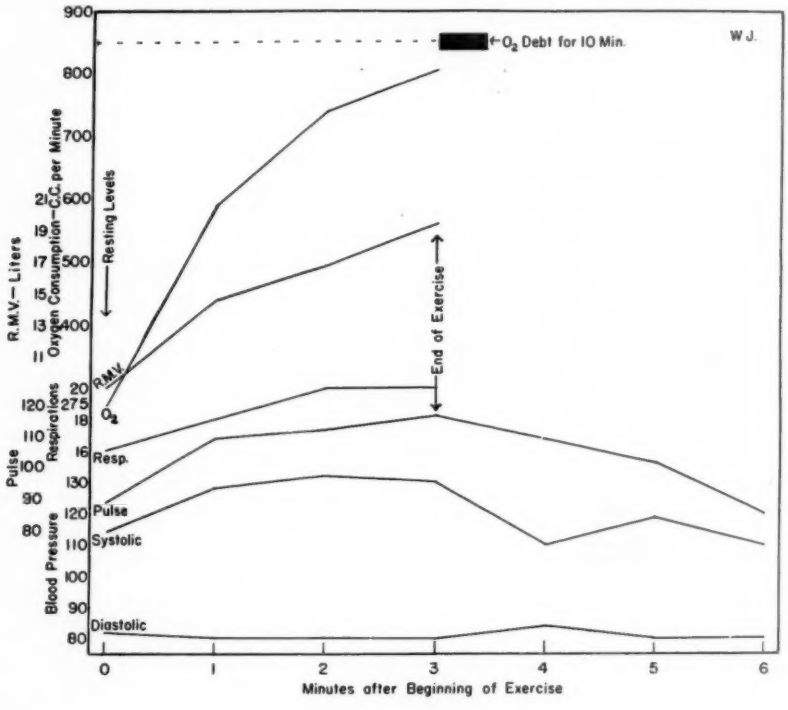

Fig. 1.

again shortly after the cessation of exercise (frequently, the pulse could not be palpated during exercise in these cases); associated with this pulse phenomenon in exercise was a low pulse pressure; (4) primary respiratory distress with rapid pulse rate, the type of response characteristically associated with cardiac weakness.

Normal Response.—The response of only one of the normal subjects is described, since it is typical of what occurred in the others. In this case (cf. Fig. 1) the respirations increased from 16 to 20 per minute, the respiratory minute volume from 9.0 to 19.3 liters per minute, and the pulse rate rose from 88 to 109 during the first, 111 during the second, and 116 during the third minute of exercise. In the third

minute after exercise it was back to 85. The oxygen consumption rose from 270 c.c. per minute before exercise to 587 c.c. per minute during the first, 738 c.c. per minute during the second, and 804 c.c. per minute during the third minute of exercise. There was an oxygen debt of 850 c.c. The blood pressure is seen to rise from 114/82 mm. Hg before exercise to 130/80 mm. Hg in the third minute of exercise. It dropped quickly after exercise to its resting level.

There was thus a slow rise in the respiratory rate, a moderate increase in pulmonary ventilation and pulse rate and a moderate rise in the oxygen consumption which in the second minute of exercise was within 10 per cent of what it was in the third. The blood pressure rose, as was to be expected, chiefly in the systolic phase so that the pulse pressure was increased. The pulse was easily palpable during the exercise.

RESPONSE IN PATIENTS WITH ANGINA PECTORIS

Failure of Pulse Rate to Rise Considerably.—In six of the patients the pulse rate failed to rise, during exercise, to the normal level. In these cases the pulse rate during exercise did not exceed 90 per minute whereas the normal rise under the conditions of our experiments was to 110 to 120 per minute. In one case the rise was from 53 to only 66 per minute. Usually the rate during exercise in this group was between 75 and 85. These are rates recorded during the first experimental period without preliminary training. In most of the cases the experiment was repeated several times. The pulse rate, instead of becoming still slower, as might be expected, either was unchanged or rose slightly. The typical response to exercise in one of the patients in this group is seen in Fig. 2. There was practically no rise in respiratory rate, the pulmonary ventilation increased somewhat, the pulse rate rose only from 60 to 81 per minute, and was 63 in the first and 58 in the second minute after exercise. The oxygen consumption rose normally, being practically the same in the second and third minutes of exercise. The oxygen debt was 520 c.c. The blood pressure did not change considerably during exercise except for a slight rise in the diastolic pressure. However, immediately after the exercise was finished, the systolic pressure rose and returned in two minutes to the level before exercise. This failure of the blood pressure (usually systolic and diastolic, occasionally only systolic) to rise during exercise was noted in two of the other three patients in this group in whom the blood pressure could be measured during exercise. In one of these patients, for example, the blood pressure before exercise was 120/80 mm. Hg; during the third minute of exercise it was 120/80 mm. Hg; in the first minute after exercise it had risen to 152/90 mm. Hg; and it remained at this level for three minutes. In the other patient in this group the blood pressure was 142/76 mm. Hg

before exercise; 142/84 mm. Hg in the third minute of exercise; 158/70 mm. Hg in the first minute after exercise; 152/78 mm. Hg in the second minute and 142/72 mm. Hg in the third minute after exercise.

The failure of the blood pressure to rise during exercise was followed by a definite rise immediately after exercise. This type of blood pressure response was noted in only one of the other patients. Wayne and Laplace[5] noted in some of their patients a rise in blood pressure after an attack of pain had been induced by stair climbing. Although pain was not produced in our cases, it is likely that we are here dealing with the same type of response to mild exercise. Cotton, Rapport and Lewis[9] observed a similar rise in blood pressure after

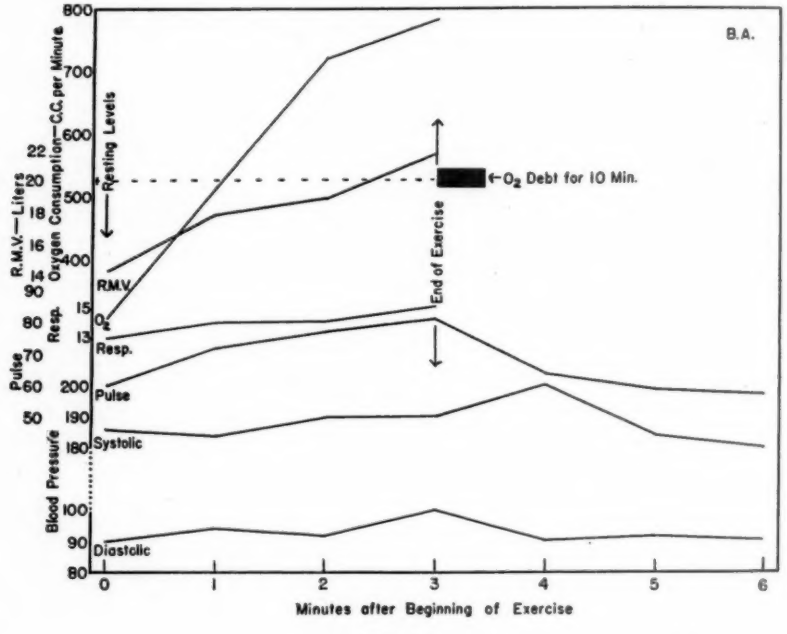

Fig. 2.

the end of exercise in some normal subjects. However, in most of these cases there was evidence of some rise in blood pressure during exercise also.

Failure of the pulse rate to rise during exercise is an interesting phenomenon capable of various interpretations. In this connection it is interesting to recall some of the clinical observations made during attacks of angina pectoris by students of the disease. Osler remarked, "Considering the increase in the respirations and the congestive state of the face and the neck, I was surprised that the pulse changed so little."[10] In Mackenzie's writings is recorded the following statement: "That attacks of great severity may be accompanied by no change in the heart action is, I think, beyond doubt."[11] Allbutt,

who apparently was intrigued by the frequent observation of the slow pulse rate during attacks of angina pectoris, graphically and in characteristic vein reminds us that "amid the agitation of patient and attendant, the heart, assumed to be the protagonist in the conflict, often seems to be the one impassive actor."[12]

Apparently the patients referred to in these quotations are in the same functional class as those under observation in this group. Occasionally, during experiments on patients in this group, cardiac pain supervened, and we found that the pulse rate remained slow. This was found to be true, also, on several occasions when some of the patients in this group were allowed to exercise until pain developed. We may, therefore, state that those patients in whom a slow pulse rate is noted during an attack probably have an abnormally slow rate during the exertion preceding and initiating the attack.

Can this slow cardiac rate in any way be responsible for the attack? Rein[13] by the use of his "stromuhr" showed that for a given amount of work the total blood flow through the coronary vessels is related chiefly to the rate of the heart and not to stroke volume or the mean arterial pressure. Other conditions being equal, the minute flow of blood through the coronary vessels is greater when the cardiac rate is more rapid. The volume of blood which flows through the coronary vessels was found to be more greatly increased when the increased cardiac output was associated chiefly with an increase in cardiac rate than when this increase in cardiac output was largely due to an increase in stroke volume. Therefore, we may assume that in the patients under discussion, a failure of the pulse rate to increase considerably during exercise may entail a less adequate blood flow through the coronary vessels. And, if we assume that cardiac pain is the result of relative myocardial anoxemia, we may conclude that the failure, in these patients, of the pulse rate to rise during exercise perhaps is an important factor in the production of the anginal attack. If the pulse rate is slow because of increased vagal tone, then the added factor of coronary constriction[14, 15] resulting therefrom might also assume some importance.

2. *Extrasystoles on Exertion.*—In two of the patients an irregular heart action developed on exertion which in one case was found by electrocardiogram to be due to auricular and in the other to ventricular extrasystoles. The general response to exercise in these two patients was otherwise not unusual. There was no abnormal response of the respiratory rate, pulmonary ventilation, or oxygen consumption. The pulse rate did not rise considerably in the case of L.K., although the rate during exercise was not considered slow enough to place this patient in the preceding group. In the case of C.E.C. the type of blood pressure response above referred to, namely a failure to rise except after exercise, was noted.

In both these cases exercise tolerance tests were performed, that is, the patients were asked to pedal at a fairly rapid rate against a pull of six pounds (395 kg. work per minute) until they experienced pain. In this manner under fixed conditions we found that on four occasions in the case of C.E.C. (cf. Fig. 3) the irregularity developed at about the same time before the onset of pain and remained for about the same time afterward. The level of the cardiac rate at which the pain developed was somewhat variable. In the other patient, L.K., these same conditions obtained, the irregularity occurring 40 to 85 seconds before the onset of pain and disappearing 30 to 70 seconds after the cessa-

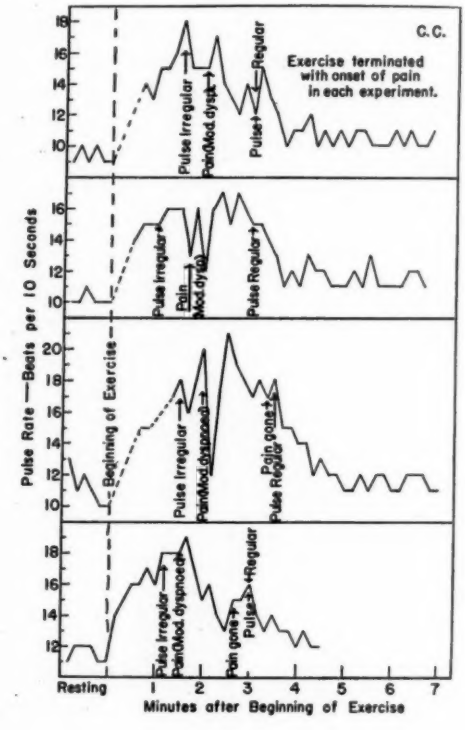

Fig. 3.

tion of exercise and after the pain had subsided or disappeared. The patients did not ride until the pain was fully developed but rather until they had the first intimation that pain was coming on. For this reason the duration of the pain was short. We were able to confirm the observations of Wayne and Laplace[5] and of Blumgart, Riseman, Davis and Berlin[16] that under constant conditions cardiac pain is brought on by a fixed amount of work, fairly regularly in a given patient.* In some of the patients presented in other groups an occa-

*This was so striking that in several patients this fact has been helpful in the diagnosis of true angina pectoris. In such cases nitroglycerin invariably increased capacity for work, whereas a saline tablet used as a control would have no effect.

sional extrasystole was found to be present in an inconstant manner after exercise or after an attack of pain. These patients, because they exhibited only rare extrasystoles and those inconstantly, are not considered in this group. In one patient, however, frequent extrasystoles were observed before, during, and after exercise, the irregularity being usually less marked during exercise. This patient will be included in this group in the discussion below devoted to therapeutic results. Wayne and Laplace noticed occasional extrasystoles at rest in a few of their patients with angina pectoris. In some they found extrasystoles when the pulse rate was approaching its normal level after exercise and often before the pain had passed off. It is quite possible that had observations been made during the exercise preceding the pain on those patients in whom extrasystoles were noticed before the pain had passed off, a relationship of the extrasystoles to the pain would have been observed similar to that recorded in our patients. Goldhammer and Scherf[17] noticed ventricular extrasystoles electrocardiographically during attacks of angina pectoris. Allbutt quotes A. Morison as observing during an attack of angina pectoris that "the pulse was not quickened but during the pain it occasionally intermitted."[18] Mackenzie[19] obtained pulse tracings during an attack which showed extrasystoles. In another case of angina pectoris Mackenzie found the heart to be "very irregular in action due to groups of idioventricular beats. It was difficult to correlate the irregularity with the attacks of pain as he was not always aware that his heart was irregular, but it was fairly evident that the pain came on with exertion when the heart was irregular."[20] Another patient of Mackenzie's observed that his attacks occurred only when his heart became irregular. He was conscious of the irregularity.[21]

It is possible that the irregularity is in some way responsible for the precipitation of the pain if we accept the view that the pain is due to myocardial anoxemia as a result of coronary insufficiency. We should also have to assume, as we may, reasonably, that the coronary flow is impaired in the presence of extrasystoles. We are inclined to the belief, as are Goldhammer and Scherf[17] that the extrasystoles in these cases are in themselves evidence of myocardial damage, perhaps increased sensitivity from a relative ischemia. In such a case the extrasystoles would tend to increase the myocardial anoxemia, and the vicious circle would end in an attack of pain. Evidence is presented below to support such a view, for when the irregularity is abolished the heart can do much more work without pain.

3. *Thin, Rapid Pulse During Exercise.*—In three of the cases the pulse during exercise became rapid, thin, and frequently barely palpable. In these cases the pulse after exercise soon resumed the full

strong character which it had manifested before exercise. The pulse rate during exercise in these cases was over 120, usually 135 to 160 although the work was relatively light (185 kg. per minute). It is noteworthy that the pulse pressure during exercise in these cases either failed to increase significantly or became smaller. Thus, in the case of E.F. (cf. Fig. 4) the blood pressure before exercise was 230/120 mm. Hg with a pulse pressure of 110 mm. Hg. In the first minute of exercise the pulse pressure was 110 mm. Hg, in the second minute

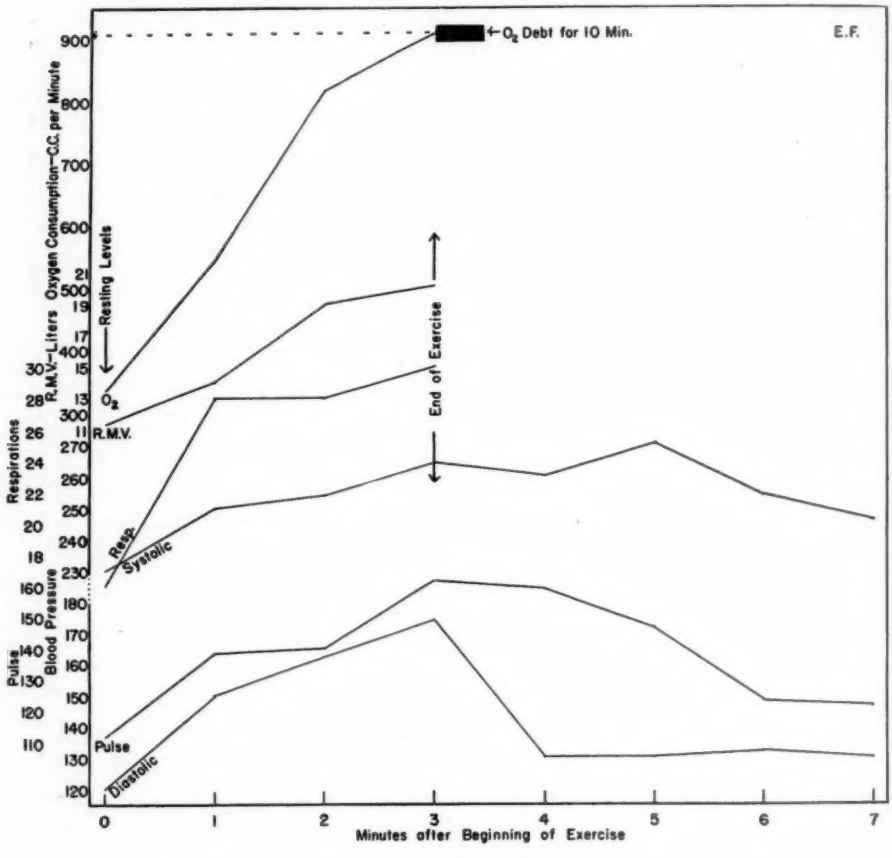

Fig. 4.

92 mm., and in the third minute 90 mm. Hg. In the first minute after exercise the pulse pressure arose to 130 mm. Hg and remained above 100 mm. during the next few minutes. The pulse rate which was rapid before exercise (112 per minute) rose to 162 during the exercise and four minutes after exercise was still 121. During exercise the pulse was frequently impalpable; at times it could barely be felt, being exceedingly thin. The oxygen consumption, pulmonary ventilation, and respiratory rates were normal during the exercise.

Perhaps it is this type of patient in whom an abnormal sensitivity exists to adrenalin as suggested by Levine, Cutler and Eppinger.[22] The type of response might suggest excessive sympathetic stimulation, being accompanied as it is by such very rapid cardiac action. This rapid action might be taken to indicate that the heart muscle is working inefficiently, for as Starling and Visscher[23] showed, the heart uses less oxygen to do a given amount of work when the rate is slow than when it is rapid. Thus a rate which is too rapid may lead to relative myocardial anoxemia and pain. Rein[13] demonstrated that for a given amount of work the coronary flow was greater when the heart rate was more rapid. The work of Starling and Visscher and of Rein might be interpreted together as indicating that as the internal work or energy expenditure of the heart is increased by an increase in heart rate, the blood flow through the coronary vessels is increased to meet this added demand for oxygen. There is thus no inconsistency in the assumption that myocardial anoxemia with resulting pain may be precipitated either because the heart rate cannot rise sufficiently (cf. group above) or because it rises too much. For, if it cannot rise adequately, the coronary blood flow and, therefore, the supply of oxygen to the myocardium do not increase sufficiently to take care of the added work of the myocardium. In this case the added work of the myocardium is due chiefly to the increased stroke volume rather than to an increased heart rate. On the other hand, if the rate is too rapid, the energy expenditure of the myocardium is so great that the coronary flow cannot be increased sufficiently to supply an adequate amount of oxygen. Thus, either an inability of the heart rate to rise adequately or a too great rise in cardiac rate may induce relative myocardial anoxemia. Therapy in either case should be directed toward obtaining a normal rate which teleologically might be assumed to be the ideal rate rather than one which is too slow or too rapid; this, of course, in addition to coronary dilatation, if that be possible. One might also speculate on the possible effect on the coronary flow of the failure of the pulse pressure to increase. Evidence in regard to the relationship of pulse pressure to coronary flow is, however, contradictory.[13, 24]

Regardless of the theoretical implications of the reactions, the fact remains that in some patients with angina pectoris the pulse rate during exercise rises to an abnormally high level; in others to an abnormally low level. In order to observe such abnormal responses it is best to employ light exercise, or exercise of such severity that normally a moderate rise in heart rate (to about 110 per minute) occurs. Then abnormally high or low levels are easily distinguishable.

4. *Dyspnea Preceding Pain.*—In three of the patients there was a definite and abnormal amount of dyspnea during the exercise. In

one patient (G.G.E.), the most striking in this group, the respiratory rate at rest was 16 per minute, the respiratory minute volume 12.6 liters. In the first minute of exercise the respiratory rate had risen to 22, the respiratory minute volume to 24.6 liters, and in the second minute of the exercise the respiratory rate had reached 36 and respiratory minute volume 36.8 liters. In the next five seconds the patient developed cardiac pain and ceased pedalling. This patient was obviously markedly dyspneic before the onset of the pain. (Pulse rate had reached 138.) Despite this, careful inquiry before the test had revealed no story of dyspnea in any way associated with his pains, and in response to a question after the test he replied that he had experienced no dyspnea. This case illustrates the inadequacy of simple inquiry in regard to information concerning the association of dyspnea with cardiac pain.

A second patient in this group, however, had noticed that he was definitely "winded" before he developed pain. In the third case, the history was indefinite.

In the two patients in this group in whom we were able to determine the oxygen consumption for the full three-minute period there was a slight delay in the increase of oxygen consumption during exercise and subsequently a somewhat greater oxygen debt (L.H. O_2 at rest 266 c.c. per minute, during first minute of exercise 300 c.c., during the second minute 527 c.c., and during the third minute of exercise 777 c.c. The oxygen debt was 1,100 c.c.). This is the type of reaction associated with cardiac weakness.[25, 26, 27]

We interpret these findings as indicating that there is primary cardiac weakness which leads to general anoxemia on exertion manifested by breathlessness which in turn leads to local myocardial anoxemia and pain. Perhaps the pain prevents too much exertion and thus too early heart failure in this group.

5. *Normal Response.*—In two of the patients the response to exercise was the same as in the normal subjects. In these cases perhaps features of the circulatory response which we did not study might have been found to vary from the normal.

Discussion of Results.—It seemed to us not so important that there were the specific groups which we have outlined as that in a relatively small number of cases so many different types of reactions should have been observed. More cases will undoubtedly reveal even more types of response.

Thus, from another angle we are once more forced to the viewpoint that angina pectoris, even the angina of effort, is merely a symptom which may be a manifestation in different people of widely different disturbances. Given a patient with the symptom of cardiac pain on exertion, it is desirable to determine what type of circulatory disturb-

ance that patient has and to attempt to direct therapy toward correcting that disturbance. Even if we assume the pain of the angina pectoris of effort always to be due to relative myocardial anoxemia, there is no reason why various factors may not produce such a state.

THERAPEUTIC INDICATIONS IN THE VARIOUS TYPES OF RESPONSES

In that group of patients in whom the pulse rate failed to rise adequately during exercise it seemed likely that we might expect some benefit from the use of atropine since atropine not only raises the resting pulse rate but allows a pulse rate to reach a higher level during a given exercise without a concomitant increase in the level of oxygen consumption for that exercise.[28] In one patient in this group on whom frequent observations were made after careful control we found that there was no increase in capacity for work when atropine was administered in doses (1 mg. subcutaneously) large enough to produce a greater rise in pulse rate during exercise than in the control period. In another patient the capacity for work without pain was perhaps slightly diminished. This patient, however, had frequent extrasystoles before and after but to a lesser extent during work. Not only were the resting pulse rate and the rate during exercise in these cases increased (average increase in rate about 20 per cent), but the rate after exercise remained considerably elevated for several minutes instead of rapidly (1-2 minutes) returning to the pre-exercise level. The usual almost immediate slowing of the pulse rate after exercise noted in this group gives to the palpating finger an impression to which Allbutt must have been referring when, in describing the pulse during an attack of angina pectoris, he remarked, "Not uncommonly, to the sensitive finger, there is to be noted in one or more beats a deliberation, an impression of delay . . . it reminds one of the momentary self-collection of a horse before he leaps."[29] This sensation, as though the pulse were holding back, was noted only after exercise. This state was abolished by atropine.

We were able to observe the effect of six weeks of absolute bed rest in one of the patients (C.J.E.) who had considerable breathlessness preceding the cardiac pain and in whom we assumed early left ventricular failure to be present. This patient received no digitalis. During the first few days of his hospital stay where he was under Dr. J. H. Pratt's care he had a definite diuresis on a Karrell diet. This was interpreted as confirmatory evidence of presence of cardiac weakness. When he was seen some two weeks after the period of bed rest, his response to exercise was essentially unchanged, there being only a slight decrease in his pulmonary ventilation and obvious breathlessness during the exercise. His field of cardiac response, as measured by the amount of work necessary to produce pain, was practically unchanged. It is obviously unfair to conclude from this one case

that prolonged bed rest is of no value in this type of case. Perhaps the addition of digitalis might help. This same patient, before he was put to bed, reported marked improvement following the use of one of the adenosin preparations. Examination indicated that though there was a subjective sense of improvement the actual amount of work he could perform under fixed conditions before cardiac pain supervened was absolutely unchanged as was the response of his cardiovascular system to exercise. This case may be taken to indicate how unreliable are simple reports of improvement based on subjective observations.

Results With Quinidine Sulphate.—In both of the patients in whom extrasystoles were found to appear just before the onset of pain and to disappear shortly after the cessation of exercise, quinidine sulphate was employed in doses up to 0.4 gram, four times a day. On the assumption that the extrasystoles decreased the effective coronary flow during exercise and hence the supply of oxygen to the myocardium, we sought to abolish the extrasystoles and thereby increase the cardiac efficiency during exercise. This was possible with quinidine.

Thus one patient (L.K.) developed cardiac pain pedalling on a stationary bicycle under the same conditions with a fixed load and at a fixed speed in from four minutes twenty seconds to five minutes twenty seconds on six occasions within one week. Two days after the last of these observations when he was taking 0.5 gram of quinidine sulphate four times daily he was able to pedal for nine minutes and forty seconds (cf. Fig. 5), and when the pain did appear, it was definitely much milder than it was during the control period. During the control period this patient regularly developed auricular extrasystoles from forty to eighty-five seconds before the onset of his pain. The irregularity persisted from thirty to seventy seconds after the exercise. With quinidine, when he was able to do twice as much work before pain developed, there were no irregularities in the pulse before, during, and after the exercise. When the quinidine was discontinued for three days, the exercise tolerance dropped to five minutes and fifty seconds, and the irregularities reappeared in the manner described above. This patient has been taking 0.4 gram of quinidine sulphate three times a day regularly for five months. His exercise tolerance, last measured after four and one-half months of quinidine therapy, remained over ten minutes (exercise was stopped at ten minutes though there was no pain). He has worked as a janitor in a large school through a very severe winter with no great discomfort, although his duties have included shoveling snow, moving barrels of ashes weighing about 100 pounds, etc. Before quinidine therapy he had been unable to carry on his work even in the warmer weather of the fall.

Quinidine not only regulated the heart rate in this patient but also caused a greater and more rapid rise during exercise as well as a slower return to the pre-exercise level. The accelerating effect of quinidine differed from that of atropine in that the quinidine caused the rate to rise more quickly, though to no higher level. The sensation of deliberation or holding back of the pulse above referred to, which was noted in both patients of this group, was abolished both by the atropine and by the quinidine. This accelerating effect was apparently in no way responsible for the improvement in capacity to work, for when this effect wore off in a few days while the patient was still taking quinidine (heart rate 102 per minute during the

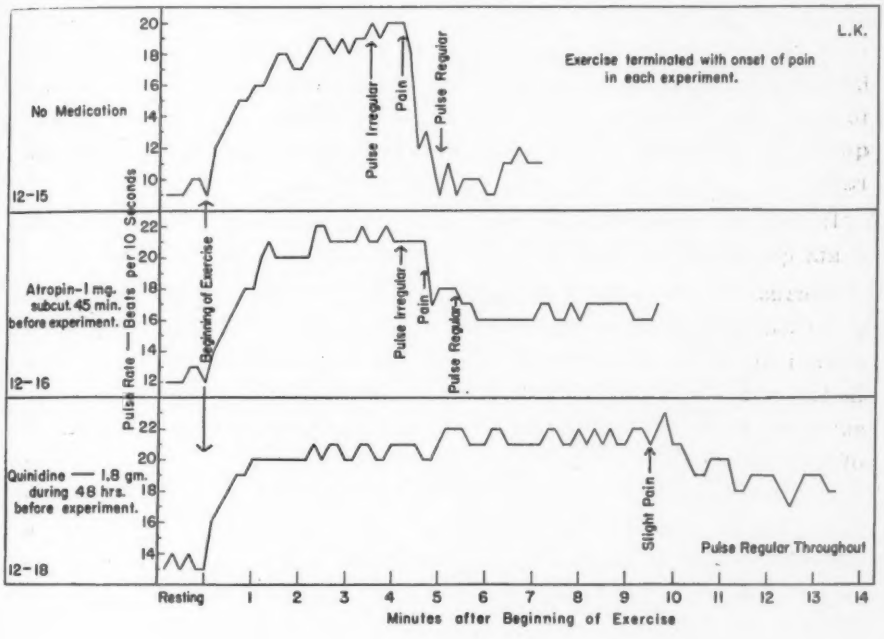

Fig. 5.

moderately severe work of the exercise tolerance test) the improvement continued. The irregularity, however, remained absent. This would indicate that it was simply the abolition of the irregularity which brought about the improvement.

A comparison of the effect of atropine and quinidine in the patient to whom we have just been referring is seen in Fig. 5 in which the quicker rise in pulse rate as well as the prolongation of the ability to perform the work is readily seen. This figure also illustrates the absence of any relationship between the level of the heart rate during exercise and the onset of pain in this patient.

The other patient who showed the same type of pulse rate response (cf. Fig. 3) developed pain on four occasions before quinidine after

pedalling 90 to 120 seconds; whereas after the irregularity had been abolished by the use of quinidine, he was able to pedal for four minutes, when he stopped because of fatigue and not because of pain. In this case, too, the pulse rate after quinidine rose more quickly to a higher level during exercise and remained at a high level for several minutes after the cessation of exercise.

In a third patient (E.L.) who had many extrasystoles before, during, and after exercise, quinidine sulphate was also given. In this case the irregularity was usually less marked during than before and after exercise. This patient was able to pedal on six occasions before the cardiac irregularity was abolished by quinidine sulphate for an average of four minutes and fifty seconds (variation three minutes, forty seconds to five minutes, twenty-five seconds). When the heart rate became regular, he was able to pedal from seven minutes, thirty seconds to eight minutes, when he stopped because of fatigue. In this case the quinidine did not have even an initial accelerating effect on the heart rate.

In two of the patients who exhibited only occasional single ectopic beats quinidine sulphate did not increase the capacity for work.

Because of the heart rate accelerating properties of quinidine the drug was given to two patients in whom there was a relatively slow pulse rate during exercise, in an attempt to learn whether the change in the pulse rate during exercise under these conditions might have some effect on the capacity for work. Since the accelerating effect of quinidine is only temporary, a prolonged effect on exercise tolerance was not anticipated. One patient (O.H.) showed no definite improvement; the other patient (L.N.) was able to double his capacity for work when his pulse rate rose more rapidly and to a greater level with quinidine. Unfortunately, only one observation could be made in this case after the control period because of the development of symptoms of quinidine intoxication. It is noteworthy that despite definite objective evidence of improvement this patient reported that he seemed no better. The fact that definitely more exertion was required to elicit the pain had not impressed itself on his mind. Even after the test when he was told he had done twice as much work as before, he seemed surprised; he simply knew that pain came on with exertion. This patient again illustrates how difficult is the evaluation of therapeutic effects in patients with angina pectoris, based on their own reaction.

On the other hand, we have one patient who kept a daily record for six weeks of the number of nitroglycerin (0.065 mg.) tablets he required for relief of pain in his daily work as a truck driver. He took the nitroglycerin only when the pain was severe. During this

period we made observations on his capacity for work under the conditions above described. A few months later when he spontaneously improved to the extent that he took no nitroglycerin for three weeks, his exercise tolerance as we measured it remained essentially unchanged. He insisted that his activities in his daily life were in no way changed and that he could definitely do more work without discomfort. The weather was essentially unchanged. This leads us to suspect that

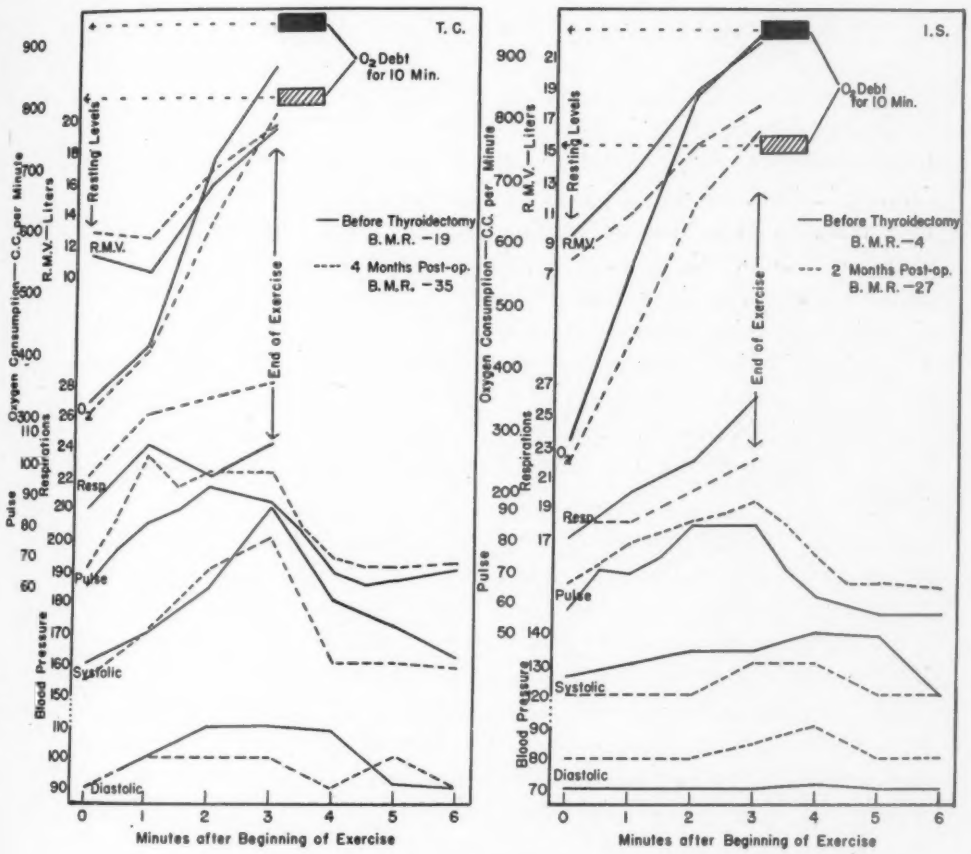

Fig. 6.

there is not necessarily a direct relationship between true clinical improvement in angina pectoris and changes in standard exercise tolerance tests.

Effect of Total Ablation of Thyroid.—Four patients with angina pectoris were studied before and after total thyroidectomy. The operations were performed by Drs. D. Berlin and E. C. Cutler of the Beth Israel Hospital and Peter Bent Brigham Hospital, respectively. In two of the patients there was considerable relief following the op-

eration; in two the relief was only slight. Examinations were made postoperatively when clinical signs of myxedema were just appearing, and, except in one case, before thyroid substance was administered. Fig. 6 represents the results in one of the two patients (T.C.) who showed definite improvement both subjectively and objectively (stair-climbing tests under Dr. Riseman's supervision at the Beth Israel Hospital) and in one of the two patients who showed only slight improvement. In both cases there was a slight decrease in the level of oxygen consumption during exercise and perhaps a slight decrease in oxygen debt (differences here recorded for oxygen debt are within the range of our experimental error). There was no significant difference in either patient in respiratory rates or pulmonary ventilation before and after thyroidectomy; neither was there any essential difference in the two patients in the response of the pulse rate to exercise, the rate in both cases reaching a higher level after the operation than before. This change in pulse rate was perhaps more striking in the patient who showed considerable improvement than in the patient in whom improvement was only slight. However, in general it can be said that there was no striking difference in the postoperative response in these two patients which might account for the difference in improvement. Perhaps the reason for this difference lies in the presence or absence of varying degrees of fixed pathological changes.

Effect of Lowering Basal Metabolism by Dietary Restriction.—Considerable interest has been attached of late to the importance of the basal metabolic rate in patients with heart disease. Total thyroidectomy has been performed in an attempt to reduce the strain on the heart by lessening the need of tissues for oxygen.[16, 22, 30]

Almost twenty years ago Benedict, Miles, Roth, and Smith,[31] in an important and comprehensive research demonstrated that a very effective and simple method of reducing the level of tissue metabolism was by the use of moderate dietary restriction over a period of several weeks. In a group of healthy young college students they were able to produce a lowering in the average basal metabolic rate of about 20 per cent by a moderate restriction in diet which led to an average loss of about 10 per cent in body weight in two months. There was thus a decrease of approximately 30 per cent in oxygen consumption. This figure was further substantiated by the fact that in the next two months the body weights remained practically unchanged with a caloric intake which was lower by approximately one-third than it was at the beginning of the experiment. It is significant that not only the level of oxygen consumption at rest but the level at work as well was lowered in the same general ratio. This change took place

with no real impairment in health. The authors made the statement, "The beneficial effects in many pathological cases of lowering the metabolism perceptibly will, it is confidently believed, be demonstrated in the near future."

It seemed to us that the pathological cases in which such a state would be extremely desirable are those with cardiac weakness. Observations are being made at present on the effects in patients with chronic myocardial disease of lowering the body metabolism by dietary restriction.[32]

It seemed also that by the use of dietary restriction we could determine whether it is the lowering of the basal metabolic rate which is responsible for the improvement which has recently been observed

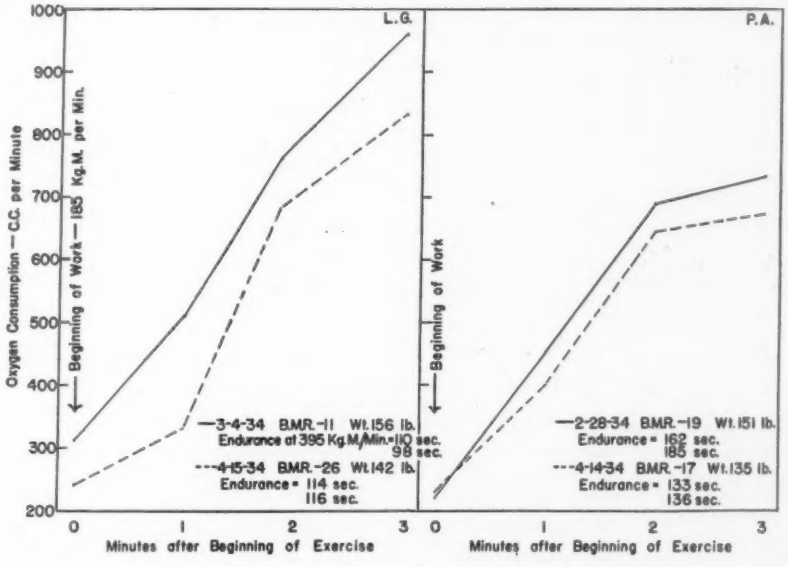

Fig. 7.

in patients with angina pectoris who have had total thyroidectomies, or some other as yet unknown change associated with the operation itself or the hypothyroid state. With this in mind, we placed two patients with angina pectoris, who apparently responded normally to the exercise tests above described. In one case (P.A.) the initial basal metabolic rate was minus 19 per cent. There was no drop in the basal metabolic rate in this patient. In the other patient (L.G.) the initial basal metabolic rate was minus 11 per cent. In this case a drop in the basal metabolic rate of 15 per cent with a loss in body weight of about 10 per cent was followed by no improvement in capacity for work. There was associated with the lowered basal metabolic rate a lower level of oxygen consumption during work, a slower pulse rate, slightly lower blood pressure at rest (no essential change

during work), and a slightly lower resting circulation time. Despite the drop in oxygen consumption and other apparently more favorable conditions for the cardiovascular mechanism, the angina pectoris remained unimproved as measured by exercise tolerance tests. The changes in oxygen consumption during work in the two patients are illustrated in Fig. 7. An adequate preliminary period of training eliminated a training effect as a source of error in interpretation.

This would indicate that some factor other than the hypometabolism is responsible for the prolonged improvement seen in angina pectoris following thyroidectomy. One of these factors may presumably be the general diminution in sensitiveness to all forms of sensation. Patients with myxedema seem slower to appreciate ordinary painful or otherwise uncomfortable stimuli, nor do they respond so acutely. Perhaps that is the reason why in two of our patients who had total thyroidectomies the remark was frequently made that even when the pain did develop it was not so severe.

SUMMARY AND CONCLUSIONS

1. Seventeen patients with angina pectoris and six normal controls in the same age group were studied in the following manner: The subjects pedalled on a stationary bicycle at a fixed load and speed for three minutes. The blood pressure, pulse rate, respiratory rate, pulmonary ventilation and oxygen consumption were measured before, during, and after (oxygen debt) the exercise. The oxygen consumption was measured during each minute of the exercise.

2. There were four general types of response in the patients with angina pectoris, the most significant disturbance in these groups being: (I) failure of the heart rate to increase normally during exercise; (II) the development of cardiac irregularity (extrasystoles) shortly before the onset of pain and its disappearance shortly after the cessation of exercise; (III) a thin, thready, rapid, barely palpable pulse during exercise associated with a failure of the pulse pressure to increase normally with a return to normal shortly after the cessation of exercise; (IV) primary respiratory distress with rapid pulse rate characteristic of cardiac weakness. In each group the disturbances might be interpreted as favoring the development of myocardial anoxemia.

3. In two of the patients the response to exercise was considered normal.

4. The variety of types of response to exercise was taken to indicate that angina pectoris is merely a symptom which may be a manifestation in different people of widely different disturbances.

5. In Group I the administration of atropine permitted the heart rate to rise to a higher level during exercise but did not increase the ca-

pacity for work without pain. In one patient in Group III absolute bed rest for six weeks was followed by no demonstrable objective signs of improvement.

6. In Group II the abolition of the cardiac irregularity by the use of quinidine sulphate resulted in a striking increase in capacity for work without pain.

7. Four patients were observed before and after thyroidectomy. Clinical improvement did not parallel changes in response to work, these changes being a slightly greater increase in pulse rate during exercise where it had been abnormally low before the operation and a lower level of oxygen consumption during exercise as well as at rest.

8. Lowering of the level of oxygen consumption at rest and during exercise by means of a prolonged restricted diet did not increase the capacity for work without pain in one patient.

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THE REESTABLISHMENT OF CARDIAC CIRCULATION DURING PROGRESSIVE CORONARY OCCLUSION*

An Experimental Study on Dogs

Harold F. Robertson, M.D.
Boston, Mass.

THERE are numerous reports of hearts having continued their functions while the coronary vessels were more or less occluded.[1-6] Four main explanations for this phenomenon are found in the literature. (Fig. 1.) First, there is the so-called "thebesian backflow" theory. Recent investigators have amplified, by excellent anatomical studies, previous records concerning vessels that run in the myocardium between the arteries and veins of the heart and the heart cavities.[2, 6-8] It has been suggested that blood might enter the heart wall from the heart cavities along these channels spoken of, respectively, as vessels of Vieussens or of Thebesius after their original discoverers.[6, 7, 10-13] Full proof that these vessels may perform this function is lacking; indeed, the explanation requires further physiological support.[14] Such a backflow into the myocardium would be quite extraordinary during systole when the intramural pressure is at least 50 mm. Hg higher than the intraventricular pressure. During diastole, pressures are more nearly equal, but whether the intracardiac pressure is ever great enough in diastole to force blood into the heart walls is still to be proved. That some ebb and flow takes place seems possible from certain data.[1, 6, 10-13] Second, there is the suggestion that a compensatory blood flow by way of intercoronary vessels, epicardial vessels, including the rami telae adiposae, and their various thoracic anastomoses through the aortic vasa vasorum, may feed the myocardium.[5] Epicardial vessels have been shown to bridge widely occluded gaps in the coronary circulation, and there is no doubt that ramifying intercoronary vessels play a major rôle in maintaining many hearts with partial occlusion.[3] Very meager evidence, however, has been presented that these vessels might receive sufficient blood from aortic vasa vasorum to sustain the myocardium when the coronaries were completely or almost totally occluded. Third, it has been suggested that venous backflow from the right auricle via the coronary sinus might suffice to nourish the heart.[2, 10] Such a sinus backflow could be for only a very brief period in each cardiac cycle because the auricle's small positive pressure barely precedes the abrupt and extensive rise

*From the Laboratory of Surgical Research, Harvard Medical School, Boston, Mass.

in coronary sinus and venous pressure which accompanies ventricular systole. As the veins were tied off in the first stage of our experiments, a test of this theory here was immediately ruled out. Fourth, it has been shown by experiment that adhesions between the heart and the thoracic viscera may carry numerous vessels to the heart wall. This method of supply is uncommon in human material, and in experimental studies such vessels played a minor rôle in the heart's blood supply.[15]

It is certain from the above data that certain hearts do receive sufficient nutrition for their functions in some way while their main source of supply is diminished. Experiments with isolated or partially isolated hearts tend to confirm this finding, the majority of workers

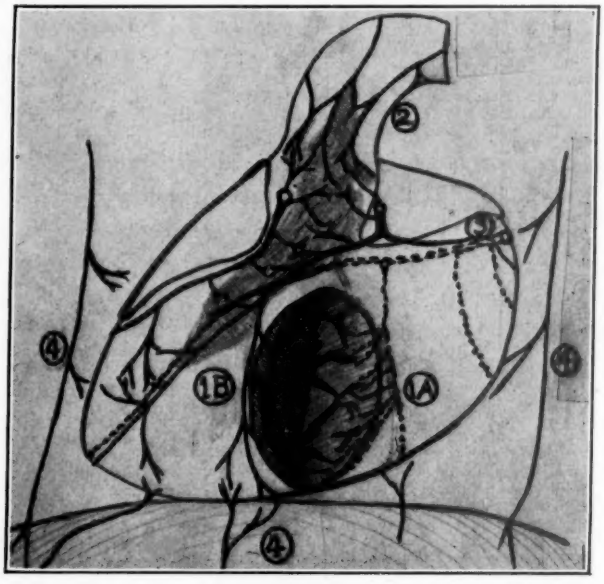

Fig. 1.—Four suggested sources of blood supply to myocardium when the coronaries are closed.
1. Backflow from heart cavities into heart wall through (*A*) vessels of Thebesius, (*B*), vessels of Vieussens.
2. Coronary vessel anastomoses through vasa vasorum of great vessels with the thoracic vessels.
3. Backflow from right auricle along coronary sinus into heart wall.
4. Vascularized adhesions between the thoracic wall, thoracic viscera and diaphragm, and the pericardium and heart.

favoring the "thebesian backflow" theory, a few adding to this the "coronary sinus backflow" theory, as the modus operandi. However, many isolated mammalian hearts may function well for some time on little nutrition, and perfusion experiments rarely parallel conditions in human material. Stella's careful experiment indicated that no backflow from the heart cavities to the cardiac vessels actually occurred in the normal heart.[14] Whether any change occurs in abnormal hearts favoring a backflow from the heart cavities into the heart wall,

awaits further proof. It, therefore, seemed reasonable to put the matter of cardiac nutrition during coronary obstruction to actual test in the living animal by producing gradual coronary occlusion and noting in what manner myocardial circulation was reestablished.

METHOD

The experimental method was as follows. The coronary sinus and the main veins of the heart were tied in from one to three stages before arterial ligature was commenced to encourage dilatation of the thebesian vessels and of the coronary vessels generally.[16, 17] The coronary arteries were then tied in several stages, the average animal having all main veins and arteries ligatured at the end of six operations. The hearts were closely watched at each stage for evidence of developing cardiac, pericardial, aortic, and thoracic anastomoses; and for any increase in the size or vascularity of the epicardial and periaortic fat pads or the pericardial fat. Finally, in the surviving dogs, the very vascular pericardial adhesions formed during these procedures were stripped from the hearts to judge what part they took in nourishing the myocardium and to see whether thebesian-like vessels, the only likely remaining source of blood supply to the heart, could support cardiac function.

A typical protocol is as follows: Dog B-98-33. Young, female police dog, 15 kg. wt. Intertracheal ether and Erlanger respirator were used throughout. Except as noted in the last procedure, the chest was always opened by intercostal incision, closure being done in layers.

Procedure I: February 20, 1933. Left chest was opened. Heart showed normal vascular distribution. Coronary sinus was tied between posterior central vein and right auricle. There was immediate bulging of sinus and all veins of left heart. Bluing of left heart wall commenced and small vessels previously invisible appeared. In five minutes arterial dilatation was moderate and petechial-like spottings were seen over the main vessels about which white fluid had gathered under the epicardium which was raised. During this time the heart rate slowed and contractility decreased. Chest was closed. Postoperative condition good. *Procedure II:* March 8, 1933. Right chest was opened. Veins of right heart were normal, anastomoses between great cardiac vein and middle cardiac vein were enlarged. Veins were tied off, heart was unaffected, chest was closed, condition was good. *Procedure III:* April 26, 1933. Left chest was reopened. Pericardium was laden with avascular fat, many vascular adhesions between vessels of pericardium and epicardial vessels of left heart, all of which were increased in number and size, especially at the apex. Great cardiac vein and anterior descending ramus of left coronary were tied just under the tip of the left auricular appendix. No change in color of heart or rate of beat. Chest was closed. Condition was good. *Procedure IV:* May 19, 1933. Right chest was reopened. Many vascular adhesions to right margin heart and about apex where the whorl of vessels was present. All branches (4) of right coronary were tied just at auriculoventricular groove. Heart slowed and contractility was lessened; there was bluing of the posterior apical region of the heart. Chest was closed. Immediate recovery was good, but later there was moderate edema of the legs lasting two weeks, then complete recovery. *Procedure V:* July 12, 1933. Left chest was reopened. Fat of mediastinal septum and pericardium markedly increased and very vascular; vascularized bands from chest wall and diaphragm to pericardium, through this to heart wall. Left marginal branches of left coronary were tied, the left coronary itself was tied without production of cyanosis or change in rhythm. Right coronary was tied. Condition was good. *Procedure VI:* August 18, 1933. Sternum was split and profuse vascular adhesions were seen from the chest wall and

diaphragm and lungs to pericardial vessels which in turn joined myocardial vessels by virtue of the adherent pericardium. Pericardium was stripped from myocardium, numerous vascular adhesions being cut and tied, leaving many patches of cyanosis. Chest was closed and dog remained well for a time with slight edema of legs. This gradually increased and after one remission of two weeks' duration the dog died in October of cardiac failure. This was the only animal to survive the last procedure of the experiment for more than a few hours.

OBSERVATIONS

Our observations will be grouped briefly under the various operative stages of the experiment. The venous ligatures were well tolerated by all animals. The left heart of some animals, when the coro-

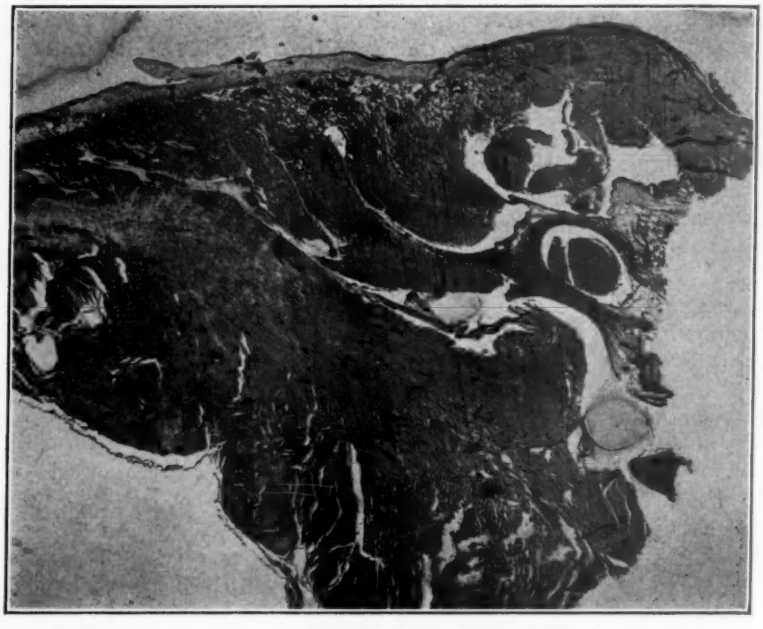

Fig. 2.—A slide from a serial section study of a heart after coronary sinus, coronary veins and coronary arteries had been tied. Arrows follow two large vessels from heart cavity through left heart wall to two epicardial vessels, one an artery, one a vein. These vessels were commonly seen.

nary sinus was tied, showed more cyanosis, more temporary venous engorgement, and a greater amount of coronary artery dilatation than did others. This variation depended on how well the thebesian vessels responded to the extra load on their ordinary function of draining the heart wall of blood not carried off by the various cardiac veins. The sinus ordinarily drains off two-thirds of the heart's blood, chiefly the left heart's. When the sinus is closed, this blood is forced into the heart cavities through thebesian channels or through the venae cordis minimae. It cannot be said definitely to what extent accessory vessels were enlarged by this procedure; but serial sections from the

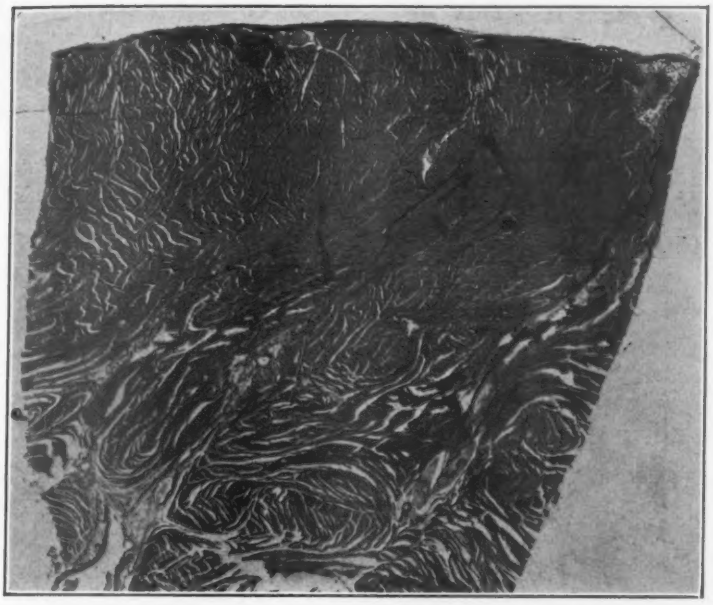

Fig. 3.—A slide from a serial section study of a heart after coronary sinus, veins, and coronary arteries had been tied. The vessels indicated by arrows penetrate the full thickness of the left heart wall, are quite dilated, and make wide anastomoses during their course.

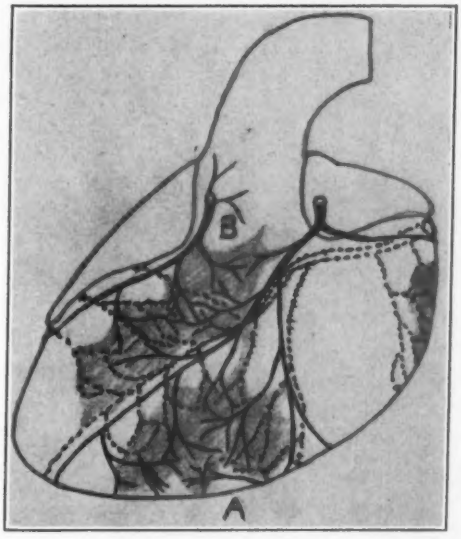

Fig. 4.—Typical areas of vascular, especially venous, enlargement and proliferation following ligature of the coronary sinus. (*A*) Apical region where veins of great cardiac vein anastomose with veins of the posterior longitudinal sulcus. (*B*) Region of conus arteriosus where branches of the great cardiac vein anastomose with right heart veins and veins of the great vessels.

hearts showed large vessels, connecting the heart cavities with the epicardial vessels, widely open at the end of the experiments (Figs. 2 and 3). By the time the main veins and any large tributaries had been tied, scanty adhesions amounting to avascular fibrinous deposits had formed between the heart and the pericardium but were easily separated. Frequently a whorl of enlarged veins was present at the apex of the heart and in other anastomotic regions such as the conus arteriosus (Fig. 4).

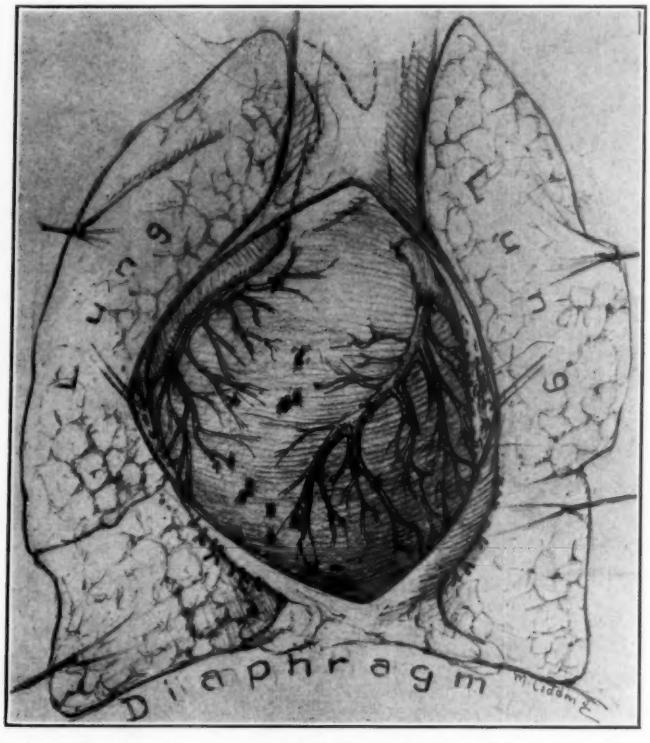

Fig. 5.—Vascular adhesions nourishing the heart wall after all vessels ligated.

Ligature of the smaller branches of the right and left main coronary stems, then the main stems, a short way from their origins, was carried out without mishap even though at the latter stage quite firm and vascular adhesions were often present which stripped from the heart with difficulty. The majority of the hearts showed a whorl of arteries and veins at the apex. This was best developed in hearts which had shown unusual cyanosis and vascular dilatation of the left heart following venous ligature. A similar change was found over the conus arteriosus. Both areas are sites where coronary anastomoses develop readily (Fig. 4). A few of the hearts showed an increase in epicardial

fat, especially in the anastomatic areas just mentioned, where venous congestion was or had been marked; but the fat was not vascularized to any extent though found in areas more vascular than usual. No evidence of increased anastomoses between the aortic vasa vasorum and the epicardial vessels was found.

The final coronary ligation closed the main trunks at their origins, any accessory vessels found being also tied. The dogs all survived this final procedure for at least some hours; the majority, however, died in twenty-four to forty-eight hours. Three suffered little or no ill effect. All the animals showed a great increase in vascularity and density of the pericardial adhesions, the vessels of which formed well-defined anastomoses between various thoracic vessels and the heart wall, especially marked along the course of the phrenic and internal

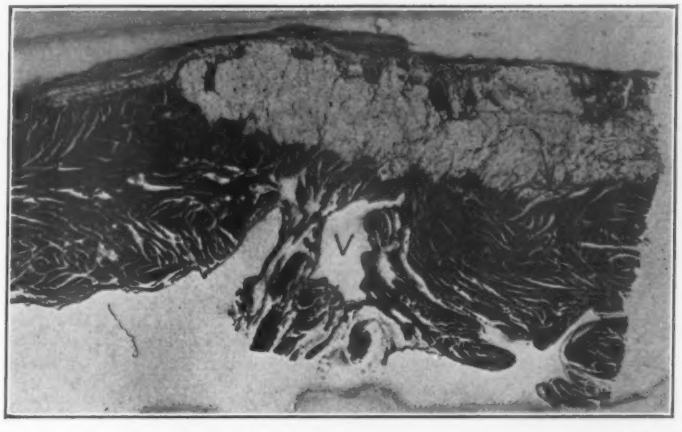

Fig. 6.—Section from heart wall after coronary artery and vein occlusion. Large channels run into the inner myocardium from the interstices between the trabeculae carnae. Although the inner heart wall is well nourished, these channels approximate an area of muscular degeneration and fatty infiltration occupying the outer half of the heart wall which they apparently could not nourish. Other sections showed degeneration of outer half of the heart wall with intact inner half of wall and no demonstrable thebesian-like vessels. The presence or absence of thebesian-like vessels seemed to have little to do with the state of myocardial nutrition.

mammary vessels (Fig. 5). These vascular adhesions were, of course, partially severed in tying the coronaries. Their separation and ligature produced definite areas of cyanosis of the heart wall. The actual ligation of the coronaries produced very little or no change in the appearance of the heart wall. As a rule, it was the animal whose heart appeared to be so largely nourished by the thoracic adhesions that survived only a short time. In these fresh infarctions were found at autopsy at points indicating that the vascular supply from other sources than the pericardial adhesions had been insufficient for cardiac vitality. It was felt that, though some trauma was done the hearts, it had not been sufficient by itself to cause the postoperative deaths.

There was no further increase in epicardial fat or epicardial anastomosing vessels, and no enlargement of aortic vasa vasorum was seen.

The three animals surviving complete coronary ligature were opened later, and the pericardial adhesions were completely separated. A definite increase in pericardial fat was found, largely avascular. There was only a slight increase in the epicardial fat over the increase seen following the first arterial closures. Prolific vascular adhesions were present arising from many sources, chiefly from the phrenic vessels, the internal mammary vessels and from pulmonary vessels which had appeared at the lung borders to grow into the pleuropericardial adhesions (Fig. 5). The separation and ligation of these vascular adhesions left areas of cyanotic heart muscle obviously infarcted. Only one animal survived the operation; the others died in twelve to twenty-four hours from typical cardiac failure. Widespread recent infarction was found at autopsy; and evidences of previous sclerosing infarctions patently from the former ligations. The one survivor developed edema of the legs with hydrothorax and a permanent auricular fibrillation. After several weeks the animal recovered for a time but edema again occurred and the animal died with all the signs of cardiac insufficiency. The heart was found to have redeveloped vascular pericardial adhesions, but areas of recent infarction were present throughout the heart muscle. The cardiac failure was not complicated by an element of adhesive pericarditis.

Microscopic sections of the hearts showed varying degrees and stages of degeneration and fibrosis of the outer heart wall. The endocardial half was nearly always well preserved, but this could not be shown to be particularly associated with the occurrence of dilated vessels of the thebesian type (Fig. 6).

SUMMARY

There were two plausible routes by which these hearts could have been nourished, by the vascularized pericardial adhesions or by the vessels of Vieussens or Thebesius. The above observations indicate that little or no nutritive function developed in those channels known as the vessels of Vieussens or Thebesius, which penetrate the myocardium from the heart cavities. Myocardial nutrition distinctly depended on the vessels contained in the pericardial adhesions. The microscopic findings, indicating little disturbance in the nutrition of the endocardial part of the myocardium, do not justify the conclusion that this part of the heart was fed by thebesian-like vessels. Intercoronary branches might have carried out this function.

There was no evidence of an anastomosis developing between the epicardial or intercoronary vessels and the thoracic vessels via the

aortic vasa vasorum to nourish these hearts. It is possible that in this experimental study the prolific vascular adhesions formed as an unavoidable sequel to the method employed superseded the development of other sources of cardiac nutrition.

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THE ELECTROCARDIOGRAM IN BROWN ATROPHY OF THE HEART*†

LOUIS N. KATZ, M.D., OTTO SAPHIR, M.D., AND HARRY STRAUSS, M.D.
CHICAGO, ILL.

ELECTROCARDIOGRAPHIC records exist in a wide variety of cardiac lesions. However, changes of the electrocardiogram in brown atrophy of the heart have apparently not been described. As a matter of fact, the literature contains no statement as to electrocardiographic records of patients who, at subsequent autopsy, showed brown atrophy of the heart. During the past year we have encountered three instances of brown atrophy of the heart, in each of which the electrocardiogram presented significant changes. In this report a short summary of the clinical, autopsy and electrocardiographic findings is given, and the significance of the electrocardiographic changes is discussed.

CASE REPORTS

CASE 1.—A white male, aged sixty years, was admitted to the hospital because of symptoms referable to peptic ulcers or gastric carcinoma. There were no significant cardiac findings elicited clinically. The autopsy revealed a primary carcinoma of the stomach. The heart was a small organ, weighing 200 grams (the body was emaciated, weighing about 92 pounds). The heart was diminished in size, about equally in all dimensions. The subepicardial fat tissue was transformed into a gelatinous material. The left ventricular myocardium measured about 7 mm. in thickness, the right 2 mm. There was some coronary arteriosclerosis. The myocardium was of a reddish brown color.

The patient died as the result of a bilateral confluent bronchopneumonia with abscess formation.

Electrocardiograms were taken as a routine procedure (cf. Fig. 1). There is a sinus rhythm. The QRS complex is small in Lead I, and inverted in Leads II and III, an appearance present in this patient for at least three years before death. Lead IV shows a small QRS, directed mainly downward.

CASE 2.—A sixty-four-year-old male was admitted to the hospital because of jaundice and pains in the abdomen radiating toward the back. The clinical diagnosis was primary carcinoma of the pancreas. There were no clinical findings significant of myocardial changes. The autopsy revealed a primary carcinoma of the head of the pancreas, with obstruction of the common bile duct and metastasis to the liver. The heart weighed 275 grams (the body was well nourished, weighing about 160 pounds). The heart was reduced in size about equally in all diameters. The subepicardial fat tissue was scanty. The left ventricular myocardium measured about

*From the Heart Station and the Department of Pathology, Michael Reese Hospital, Chicago.

†Aided by the Frederick K. Babson Fund for Diseases of the Heart and Circulation.

12 mm. in thickness, that of the right 2 mm. There were moderate arteriosclerosis of the coronary vessels and slight myocardial fibrosis. The heart muscle was deep brown.

The patient died as the result of a pulmonary embolus arising from a thrombus in the common iliac vein.

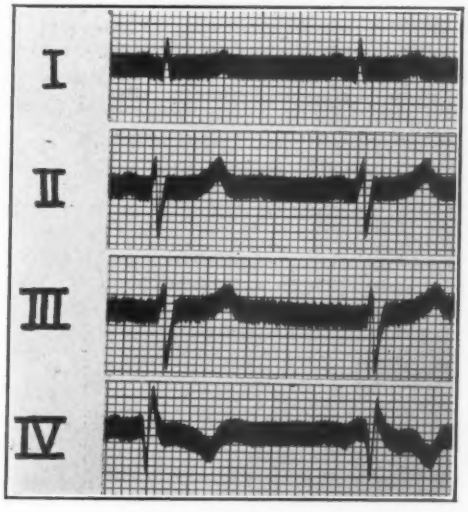

Fig. 1.

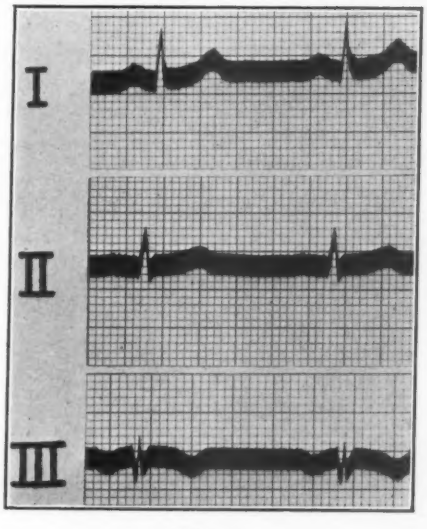

Fig. 2.

The electrocardiogram (Fig. 2) shows a sinus rhythm and occasional auricular extrasystoles, small amplitude of QRS in Leads II and III, and a relatively small amplitude in Lead I. The T-wave is inverted in Lead III. The record shows a slight left axis shift, but the changes are all within normal limits.

CASE 3.—A forty-five-year-old male was admitted to the hospital because of a diffuse enlargement of the lymph nodes and evidence of portal obstruction. There were no clinical symptoms referable to myocardial changes. At autopsy there was a lymphosarcoma involving the mesenteric, retroperitoneal, inguinal, tracheobronchial, and cervical lymph nodes, the spleen, liver and kidneys. The heart was distinctly atrophic, weighing only 250 grams (the body weighed about 180 pounds). The heart seemed uniformly reduced in size. The subepicardial fat tissue was transformed into a gelatinous material. The myocardium was dull, deep brown, and soft. The right ventricular myocardium measured 1 mm. in thickness, the left 8 mm. The coronary arteries were patent throughout. There was only a slight coronary arteriosclerosis.

The patient died of a bilateral confluent bronchopneumonia.

The electrocardiogram (Fig. 3) shows a sinus rhythm, QRS inverted in Lead III, and QRS relatively small in Leads II and III. The T-wave is small in Lead III. There is a left axis shift but the record is within normal limits.

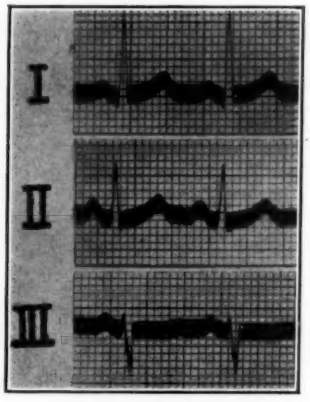

Fig 3.

It is interesting that in each case there was left axis shift, in Case 2 slight, in Case 3 moderate, and in Case 1 marked. A record such as that obtained in Case 1 is customarily considered *prima facie* evidence of a left ventricular preponderance and presupposes a hypertrophied heart. It was, therefore, a surprise to find the heart, at autopsy, actually smaller than normal. It is true that in each of these hearts there were other cardiac lesions present, but none of these can explain the axis shift. There was no evidence of any obviously altered position of the heart to account for the axis shift. Perhaps the axis shift came about because the reduction in size was less in the left than in the right ventricle, but the evidence obtained post mortem is not clear-cut on this point.

It follows from this observation that left axis deviation, even of advanced degree, is not in itself evidence of hypertrophy, but it may occur not only in a normal sized heart but also in an atrophied one.

SUMMARY

The electrocardiograms in three instances of brown atrophy of the heart are described. Emphasis is placed on the occurrence of left axis deviation in each of these records. Left axis deviation, even of advanced degree, cannot therefore be taken by itself as evidence of cardiac hypertrophy since it can occur in an atrophied heart.

EFFECT OF DIGITALIS ON THE APPEARANCE OF LEAD IV*†

HARRY STRAUSS, M.D., AND LOUIS N. KATZ, M.D.
CHICAGO, ILL.

IT HAS been shown that in recent coronary occlusion characteristic diagnostic changes are to be found in Lead IV of the electrocardiogram.[1] In view of the rapid changes commonly occurring in the ordinary leads following the administration of large quantities of digitalis, it appears not unlikely that the contour of Lead IV also may be altered by digitalis. In fact, on several occasions the interpretation of changes in Lead IV has been complicated by the fact that the patients had been receiving digitalis. We therefore decided to study the effect of digitalis on Lead IV.

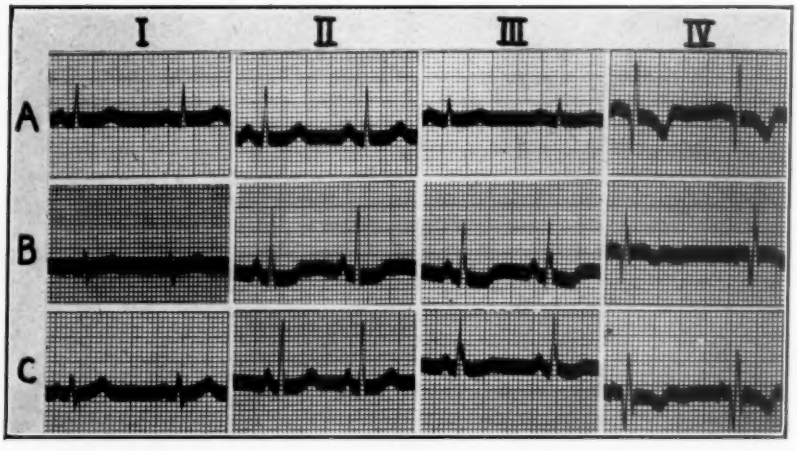

Fig. 1.—Four lead electrocardiograms obtained in Subject 1 (Table I): *A*, control; *B*, segments taken one day after digitalis was stopped; *C*, segments taken three days after digitalis was stopped (note the persistence of some of the changes in segment *C*, also the right axis shift).

The present report deals with such a study on 13 subjects, 7 being normal individuals in whom digitalis intoxication was experimentally induced and the other 6 being cardiac patients with various types of lesions, in whom digitalization was demonstrable clinically and in the standard three leads of the electrocardiogram. The procedure in the normal individuals was to digitalize them up to the point of toxicity and to compare the appearance of the four-lead electrocardiograms taken at this time with the contour before digitalis was started. Additional records were also taken for comparison at intervals after

*From the Heart Station, Michael Reese Hospital, Chicago.
†Aided by the Frederick K. Babson Fund for Diseases of the Heart and Circulation.

stopping the digitalis. Four-lead records were taken in the cardiac patients at the height of the digitalization and at various intervals after digitalis had been stopped.

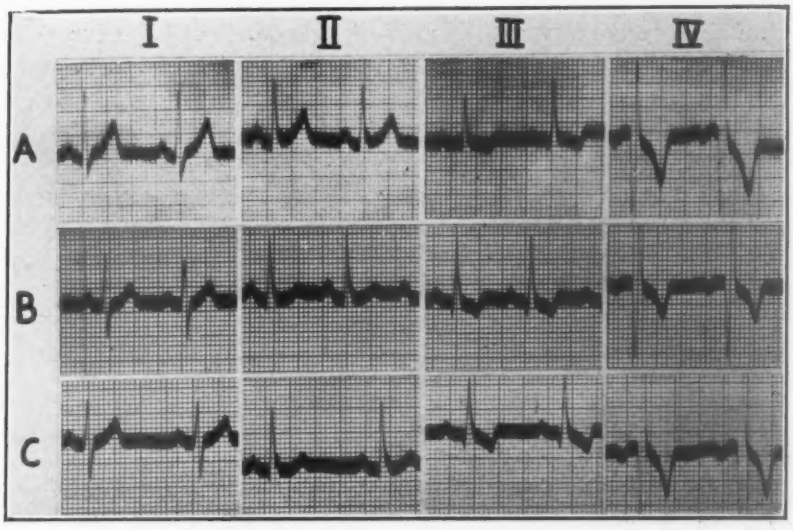

Fig. 2.—Four lead electrocardiograms obtained in Subject 5 (Table I): *A*, control; *B*, segments taken one day before digitalis was stopped; *C*, segments taken three days after digitalis was stopped.

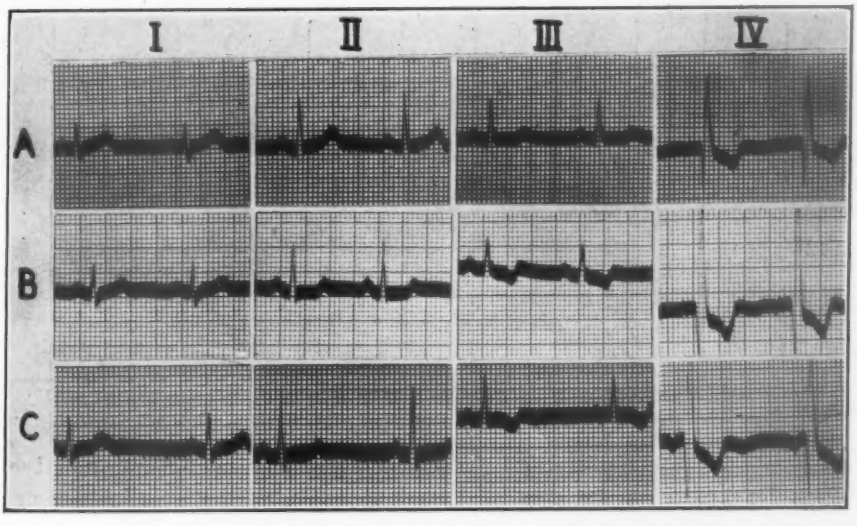

Fig. 3.—Four lead electrocardiograms obtained in Subject 7 (Table I): *A*, control; *B*, segments taken one day after digitalis was stopped; *C*, segments taken eight days after digitalis was stopped.

The results obtained are briefly summarized as far as Lead IV is concerned in Table I and illustrative curves shown in Figs. 1 to 4. The chief changes seen in Lead IV were in the S-T segment and T-

wave, and these were reversible on discontinuing the digitalis. The changes in the S-T segment in Lead IV were variable. It became positive in 5 instances (cf. Figs. 1 and 4), depressed in 4 (cf. Fig. 3), and unchanged in 3 (cf. Fig. 2). In one instance the S-T changed from a slightly negative to the isoelectric level. The negative T-wave in Lead IV became smaller in every instance (cf. Figs. 1, 2, and 3),

TABLE I

CHANGES IN LEAD IV PRODUCED BY DIGITALIS

SUBJECT NO.	DIGITALIS		CHANGES IN LEAD IV FOLLOWING DIGITALIS		REMARKS
	AMOUNT TAKEN GRAINS*	TAKEN OVER DAYS	S-T SEGMENT	T COMPLEX	
1	24	3	Became positive	Became smaller	Normal
2	27	3	Became negative	Became smaller	Normal
3	24	4	No change	Became smaller	Normal
4	39	9	Became isoelectric	Became smaller	Normal
5	45	5	No change	Became smaller	Normal
6	30	5	No change	Became smaller	Normal (inactive rheumatic heart disease)
7	36	3	Became negative	Became smaller	Normal
8	42	14	Became positive	Disappeared	Aged 40. Rheumatic heart disease, auricular fibrillation.
9	94	21	Became positive	Disappeared	Aged 44. Rheumatic heart disease, congestive heart failure, auricular fibrillation, pulsus bigeminus, complete A-V block.
10	54	9	Became negative	Became positive	Aged 55. Diabetes mellitus, hypertension, congestive heart failure, sinus rhythm.
11	26	9	Became negative	Became smaller	Aged 52. Diabetes mellitus, coronary sclerosis, sinus rhythm.
12	40	7	Became positive	Became smaller	Aged 60. Coronary sclerosis, hypertension, auricular fibrillation.
13	189	42	Became positive	Became smaller	Aged 53. Hypertension, auricular fibrillation, complete A-V block.

*Burroughs and Wellcome powdered leaf (or its equivalent), 1½ grains = 1 cat unit.

in 2 it disappeared entirely (cf. Fig. 4), and in one it became positive. The changes in the S-T and T complexes following digitalization are rapid and, on occasion, rather striking. In several instances, particularly in patients with heart disease, the contour in Lead IV closely resembled the contour seen following recent coronary occlusion (viz., Fig. 4). Since digitalis can produce changes resembling those seen in recent coronary occlusion, it is important to determine whether or not digitalis has been given in a particular patient before arriving

at a final diagnosis. A final evaluation may sometimes depend on comparing the records with those obtained following a subsequent digitalization.

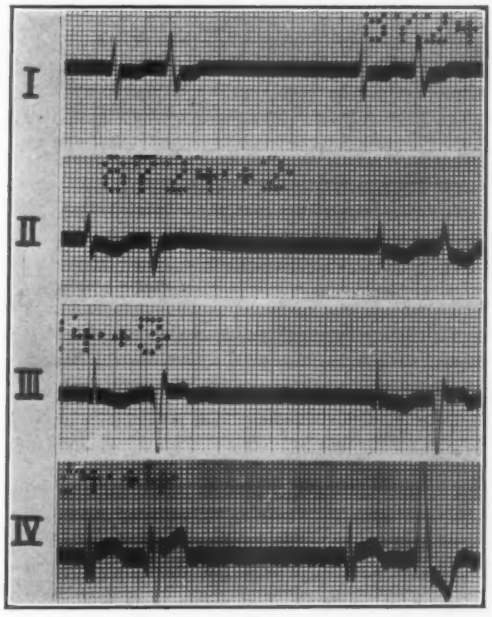

Fig. 4.—Four lead electrocardiograms taken during digitalis intoxication in Subject 9 (Table I). (Note the complete A-V block and the bigeminus with ventricular extrasystole from several foci.)

SUMMARY

Digitalis in large doses produces rapid changes in Lead IV which occasionally resemble, and consequently must not be confused with, those seen in recent coronary occlusion.

We are grateful to the volunteers who acted as subjects for this experiment. Since this communication was submitted for publication, we have seen thirteen more instances of digitalis distortion of Lead IV. In several the problem of differentiating the change from that due to a recent coronary occlusion presented considerable difficulty.

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GALLBLADDER-HEART REFLEXES IN MAN UNDER SPINAL ANESTHESIA*†

RALPH B. BETTMAN, M.D., AND S. H. RUBINFELD, M.D.
CHICAGO, ILL.

CARDIAC irregularities in gallbladder disease are clinically important. Years ago Babcock[1] called attention to the frequency of myocardial incompetence associated with chronic cholecystitis, which was alleviated following operative relief of the gallbladder condition. He offered as the most likely explanation a reflex action resulting from irritation of the splanchnic and pneumogastric filaments distributed to the wall of the gallbladder.

Osler[2] pointed out that patients with biliary colic may die of cardiac standstill. Mayo[3] and others have observed cardiac arrhythmias associated with biliary tract disease. Straus and Hamburger[4] reported 4 cases of diseased gallbladders associated with definite cardiac irregularities, shown either by electrocardiograph or pulse. In 3 of the cases the irregularities disappeared postoperatively. Buchbinder[5] demonstrated that the sudden release of bile from an incised frog's gallbladder was attended by transient arrest followed by sinus bradycardia. He concluded that a specific reflex to the heart, of vagal origin, is initiated from the gallbladder, and this is perhaps the basis for the arrhythmias in man with gallbladder disease. With reference to the reflexogenic nature of this phenomenon, Allen[6] showed that the pathway of impulses causing pulsus bigeminus in rabbits after insufflation of benzol came from the vicinity of the hypothalmus and the superior colliculus. Brow, Long and Beattie[7] produced extrasystoles and tachycardias, which disappeared after experimental removal of the stellate ganglion and severance of the portion of the brain which lies between the caudal end of the optic chiasm and the cephalic end of the superior colliculus. Recently Scott and Ivy[8] confirmed the work of Carlson and Luckhardt[9] and the Buchbinder phenomenon, but concluded that the latter was due to the irritant action of bile on the peritoneum. They noted no change under manipulation of the gallbladder, although the mechanical stimulation of other viscera caused cardiac inhibition. Schrager and Ivy[10] consider that the functional status of the cardiovascular system is the determining factor in the reaction from distention of the biliary passages. Crittenden[11] recently showed that cardiac arrest, heart-block, and slowing follow vomiting

*Aided by the Emil and Fanny Wedeles Fund of the Michael Reese Hospital for the Study of Diseases of the Heart and Circulation.

†From the Heart Station and the Gall Bladder Group, Michael Reese Hospital, Chicago.

induced by apomorphine; also that the heart rate in normal students increased after swallowing of stomach tubes.

The application of these experimental methods to man is not mentioned in an extensive review of the pertinent literature except for a recent report by Maher and his associates.[12] The reaction of the heart to surgical manipulations of the abdominal organs, particularly the gallbladder, is a matter of importance to the internist and the surgeon. The present report deals with the electrocardiographic manifestations during cholecystectomy under spinal anesthesia.

METHOD

The study includes a consecutive series of 17 patients with clinically proved gallbladder disease, who were subjected to operation for removal of the gallbladder. Two of the patients presented clinical evidence of slight myocardial impairment due to rheumatic or to arteriosclerotic heart disease. None of these cases was known to present any clinical evidence of cardiac arrhythmia.

TABLE I

HEART RATE CHANGES DURING GALLBLADDER MANIPULATIONS*

NO. TRIALS	PROCEDURE	ACCELERATION		SLOWING		NO EFFECT
		NO. CASES	CHANGE IN RATE PER MIN.	NO. CASES	CHANGE IN RATE PER MIN.	NO. CASES
16	Anesthesia	11	6-84	4	13-27	1
12	Pressure on gallbladder	4	7-12	2	12-15	6
11	Clamping and pulling on gallbladder	6	6-38	2	11-43	3
3	Release of gallbladder tension	1	21	2	8-11	0
12	Occlusion of cystic duct	2	8-34	6	7-41	4
10	Removal of gallbladder	4	13- 2	4	13-24	2
8	Pressure on right kidney	2	9-20	3	16-56	3

*Changes of less than 6 beats per minute were considered within the limits of experimental error.

Spinal anesthesia was used in all cases. The spinal anesthetic employed was either spinocain or nupercain, in the dosage of about 250 mg. properly injected at the level of the first or second lumbar interspaces. Effective anesthesia was obtained as high as the level of the first thoracic, and was tested by means of a sharp instrument applied to the operative field fifteen to twenty-five minutes after the administration of the drug.

The usual arrangement to take electrocardiograms was made, care being observed to avoid the operative field. The electrocardiograms were recorded on a mobile machine brought directly into the operating room. Records were taken before and after effective anesthesia and during the various steps of the usual cholecystectomy, with control readings before and after each step whenever possible. It was not always feasible to obtain control records because of the danger to the patient of prolonging the operation.

The electrocardiographic records were studied with respect to (A) rate changes, (B) arrhythmias or ectopic beats.

A. Rate changes are presented in Table I. The results are variable, but the usual effects of anesthesia, pressure, clamping and pulling on the gallbladder were to increase the heart rate over control periods. On the other hand, both the release of gallbladder tension and the occlusion of the cystic duct usually caused inhibition of the heart. The effect of pressure on the kidney was variable.

B. Arrhythmias or ectopic beats. In the entire series, 3 patients developed cardiac irregularities during the operation; 2, ectopic beats; and 1, sinus arrhythmia. One patient, in whom ectopic beats were present, showed an increase in their frequency during the operation. Two of the patients developed ventricular extrasystoles, one during the ligation and cutting of the cystic duct and artery, the other during the period of pressure on the gallbladder. Two patients showed ectopic beats of nodal origin, in one during the initial control record and in the other only during the period of tested effective anesthesia. The former patient had ventricular extrasystoles during the period of tested effective anesthesia and pressure on the gallbladder; in the latter sinus arrhythmia was evident after the anesthesia became effective.

SUMMARY

Sixteen cases of proved galibladder disease were studied during cholecystectomy under spinal anesthesia by consecutive series of electrocardiograms during the usual stages of the operation. The usual effects of pressure, clamping, and pulling on the gallbladder were to increase the heart rate. Only two of the sixteen patients developed ectopic beats during operation. One having such ectopic beats before operation showed an increase in their frequency during operation. One instance of sinus arrhythmia developed during the operation. These changes are taken to indicate reflex effects on the heart from the operative field.

We wish to express our thanks to Dr. L. N. Katz for his guidance and criticism.

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Department of Clinical Reports

A CASE OF SINO-AURICULAR BLOCK AND ALMOST COMPLETE A-V DISSOCIATION WITHOUT PRIMARY A-V BLOCK*†

HARRY STRAUSS, M.D.
CHICAGO, ILL.

AN UNUSUAL type of cardiac arrhythmia is reported because of the rarity of its occurrence and the difficulty of its interpretation. The interpretation was arrived at after the records were analyzed according to the method developed by Zeisler in this laboratory.[1]

The records of this patient are shown in Fig. 1. The P-P intervals are given in the top lines and the R-R intervals in the bottom lines above each record. The oblique lines represent the R-P and P-R intervals. Conducted beats are shown by heavy oblique lines with arrows. In Leads II, III, and IV there is overlapping where long strips had to be cut for illustration.

In attempting to unravel the mechanism attention was first paid to the P-P intervals; it was soon evident that the P-P intervals fell into 4 groups (see Table I), having a least common denominator (a value in the neighborhood of 0.57 sec.). This indicates that this is a case of S-A block, the ratio of conducted sinus beats varying from 1:1 to 4:1. The variations in the P-P intervals in each group are due to the presence of a moderate sinus arrhythmia with shifting pacemaker as shown by the variation in contour of the P-wave, especially seen in Leads III and IV (Fig. 1).

The long pauses between sinus beats permit frequent nodal escapement. The intervals before the A-V node discharged vary considerably, indicating that this node also has an arrhythmic discharge. This is not usual in nodal escape. The P-wave following the nodal escape often reached the A-V node and bundle during its refractory period (interference dissociation). When the P-wave reached the A-V junctional tissue a little later, it was conducted through usually with a normal but occasionally with a prolonged P-R interval (see Table II). Twice this prolonged P-R interval (0.24 second) was present with a relatively long preceding R-P interval (0.84 and 0.78 sec.). It may

*From the Heart Station, Michael Reese Hospital, Chicago.
†Aided by the Frederick K. Babson Fund for Diseases of the Heart and Circulation.

be that in these two instances the A-V node and bundle were still relatively refractory when the auricular impulse reached them. There is a wide variation in P-R interval, not dependent on the R-P interval duration, associated, in part at least, with the shift in the auricular pacemaker.

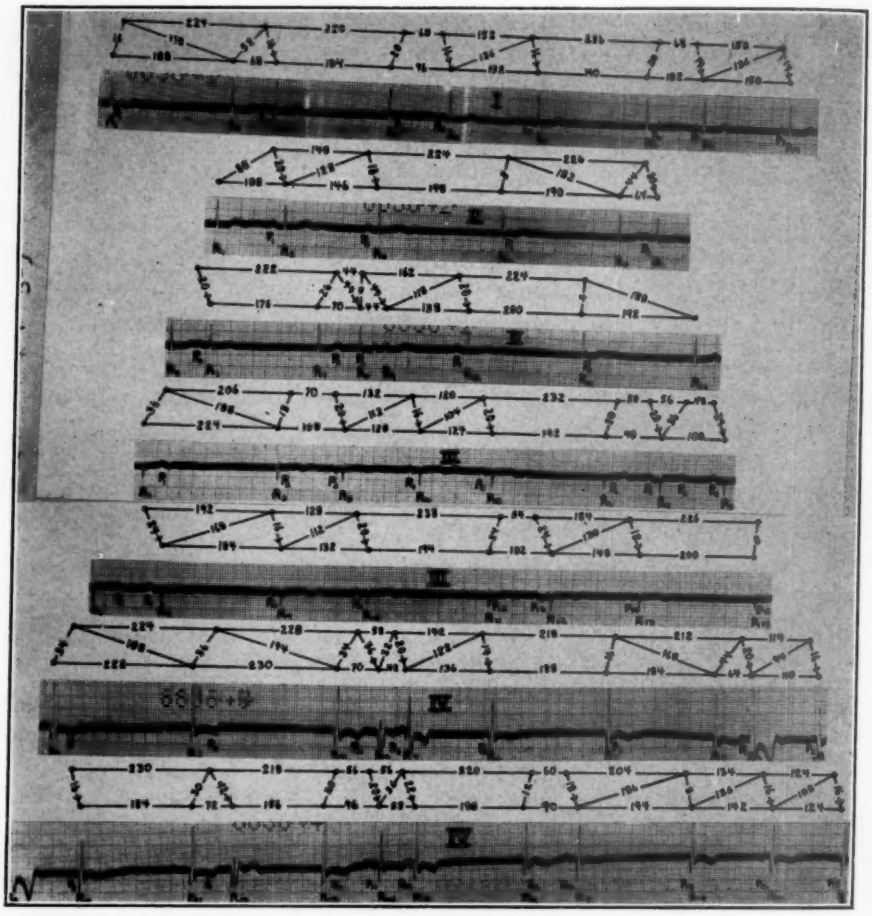

Fig. 1.

Two interesting instances of conducted beats are P_4-R_5 in Lead IV and P_6-R_5 in Lead II. The former is an instance of very short R-P interval with a normal conduction time, whereas other beats with the same R-P interval have prolonged P-R intervals or show blocked P-waves. The latter, with an R and P simultaneous, when it might be anticipated that the P-wave would be blocked out, in this instance was conducted through. Both of these beats occurred immediately following two ventricular beats in quick succession. These are not

TABLE I

P-P INTERVALS ASSEMBLED ACCORDING TO VIEW AS TO MANNER OF S-A CONDUCTION

	1:1 SEC.	2:1 SEC.	3:1 SEC.	4:1 SEC.
	0.60	1.32	1.52	2.24
	0.68	1.20	1.50	2.20
	0.44	1.28	1.48	2.26
	0.70	1.14	1.62	2.24
	0.50	1.34		2.26
	0.56	1.24	1.54	2.22
	0.48		1.42	2.24
	0.54			2.06
	0.58			2.32
	0.56			1.92
	0.56			2.38
	0.60			2.26
				2.24
				2.28
				2.18
				2.12
				2.30
				2.18
				2.20
				2.04
Average P-P Interval	0.57	125 = 0.62 × 2	1.51 = 0.54 × 3	220 = 0.55 × 4
Variation	0.44 – 0.70	1.14 – 1.34 = (0.57 – 0.67) × 2	1.42 – 1.62 = (0.47 – 0.64) × 3	192 – 238 = (0.48 – 0.60) × 4

TABLE II

RELATION OF P-R TO R-P INTERVAL, ARRANGED ACCORDING TO R-P INTERVAL DURATION

R-P INTERVAL SEC.	P-R INTERVAL SEC.	R-P INTERVAL SEC.	P-R INTERVAL SEC.
1.68	0.16	0.44	0.20
1.36	0.16	0.44	0.20
1.36	0.14	0.36	0.22
1.30	0.18	0.36	–*
1.28	0.18	0.34	0.36
1.26	0.16	0.34	–
1.22	0.14	0.30	0.42
1.18	0.20	0.26	0.44
1.12	0.16	0.24	–
1.12	0.20	0.22	0.20 $P_4 - R_5$ (IV)
1.08	0.16	0.20	–
1.04	0.20	0.20	–
0.94	0.16	0.20	–
0.88	0.20	0.20	–
0.88	0.20	0.18	–
0.88	0.14	0.16	–
0.84	0.24 $P_9 - R_8$ (III)	0.16	–
0.80	0.16	0.12	–
0.78	0.24 $P_{12} - R_{12}$ (III)	0.08	–
0.76	0.20	0.08	–
0.72	0.18	0.04	–
0.70	0.20	0.00	0.44 $P_6 - R_9$ (II)
		–0.08	–

*Blocked out.

instances of a supranormal phase but are in all probability due to the improvement of the nourishment of the junctional A-V tissues shortening the refractory period.

Aberrant conduction was found when a ventricular beat occurred soon after its predecessor, viz., R_9 Lead II, R_4, R_5 and R_{12} Lead IV, when it might be expected that the impulses would reach the conduction system of the ventricles during their relative refractory phase.

SUMMARY

An unusual case of cardiac arrhythmia is presented which shows sino-auricular block of varying degrees, 2:1, 3:1 and 4:1, almost complete A-V dissociation without primary A-V block, nodal escapement, aberrant conduction, and sinus arrhythmia with shifting pacemaker.

This case illustrates the advantages of the method of analysis developed in this laboratory in aiding the interpretation of such cases.

It is a pleasure to express my indebtedness to Dr. Louis N. Katz, at whose suggestion this analysis was made, for his helpful advice and criticism. We are indebted to Dr. M. Lev, whose patient this was, for permitting us to take these electrocardiograms. A second electrocardiogram taken six months later showed similar disturbances.

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Department of Reviews and Abstracts

Selected Abstracts

Schneider, Edward C., and Crampton, C. B.: The Effect of Posture on the Minute Volume of the Heart. Am. J. Physiol. 110: 14, 1934.

Using the Grollman acetylene method, the minute volume of the heart has been studied on seven healthy male subjects to determine the effect postural change in the body may have on the heart output. From this study the authors conclude that the minute volume of the heart is increased in the recumbent as compared with the erect position.

Ordinarily on prolonged quiet standing the output of the heart either remains unchanged or decreases slightly in subjects displaying no distress as a result of the long standing. The heart output is decreased in subjects who on long quiet standing display poor circulatory compensation in the erect position. A pulse pressure below 20 mm. of mercury indicates a falling cardiac output.

Lisa, James R., and Chandlee, Gertrude Jackson: The Heart and Great Vessels in Combined Syphilitic and Rheumatic Infection. Arch. Int. Med. 54: 952, 1934.

The lesions and the clinical course in six cases of combined syphilitic and rheumatic infection of the heart and great vessels were mainly rheumatic. In one case only was the rôle of syphilis of equal importance to that of rheumatic infection. The combined active infections carry a much graver prognosis than either infection occurring separately. Heart sounds help in the differential diagnosis of rheumatic and syphilitic aortic disease. Roentgenology is a valuable aid in the differential diagnosis between the rôles of syphilis and rheumatic infection in the production of cardiovascular pathologic processes. Syphilis of the myocardium could not be proved in any of the cases.

Graybiel, Ashton, Allen, Arthur W., and White, Paul D.: A Histological Study of the Arterioles of the Muscle and Skin From the Arm and Leg in Individuals With Coarctation of the Aorta. J. Clin. Investigation 14: 52, 1935.

It was found that the hypertension associated with coarctation of the aorta in five young individuals did not cause sclerosis of the arterioles or smallest arteries of the skin or voluntary muscles. In the five cases, the systolic blood pressure in the arm averaged 70 mm. more than that in the leg and the diastolic pressure in the arm 28 mm. more than that in the leg. Nevertheless, it was impossible by biopsy in these cases to distinguish the arterioles and smallest arteries of the arm from those of the leg.

Bishop, Paul A., and Roesler, Hugo: The Roentgenologic Diagnosis of Intracardiac Calcifications. Am. J. Roentgenol. 31: 1, 1934.

The frequency of postmortem findings of calcification of the left-sided annuli fibrosi and the aortic and mitral valves is cited. Attention is called to the few reports of the roentgen observation of these calcifications in the living and the

rarity of correct diagnosis of their location. Three such cases are reported, all of them confirmed by autopsy study. The characteristic features of appearance, location, and motion of these shadows in roentgenoscopic study are described, together with points of differential diagnosis. The technic for making films to show the calcification is described.

It is the authors' belief that these calcifications are more frequent than is realized and that the roentgenologist can play the leading rôle in their recognition by routine roentgenoscopic observation of the heart in routine chest examinations. Some physiologico-pathological aspects of this type of calcareous degeneration are described, together with illustrative cases from the literature.

Scupham, George W.: Effect of Theobromine on Peripheral Vascular Disease. Arch. Int. Med. **54**: 685, 1934.

Theobromine and its salts, particularly theobromine sodium acetate, act as peripheral vasodilators and are useful in the treatment of peripheral arteriosclerosis and early cases of thromboangiitis obliterans in which there is a large element of angiospasm. Their use results in subjective improvement in intermittent claudication, and repair of loss of tissue integrity has been noted. These drugs are not effective in all cases, but the results obtained with them are sufficiently good to make them a valuable adjunct in the treatment of peripheral vascular diseases.

Nahum, L. H., and Hoff, H. E.: The Effect of Injection of Monoiodoacetic Acid and Sodium Cyanide on the Mammalian Heart. Am. J. Physiol. **110**: 56, 1934.

Experiments were undertaken to study the effect on the electrocardiogram of poisoning with monoiodoacetic acid, which prevents the accumulation of lactic acid and sodium cyanide which promotes such accumulation of lactic acid.

It is believed that the failure of the anaerobic energy system of the heart induced by monoiodoacetic acid leads to an acceleration in heart rate, a decrease in conduction time, and a reduction of the duration of the ventricular complex as well as to profound alterations in the ventricular complex characterized by a change in the direction of the T-wave, disappearance of the isoelectric interval, and displacement of the S-T segment.

The suppression of oxidations by cyanide results in marked slowing of the heart rate, gradual development of A-V block and prolongation of the duration of the ventricular complex without further permanent changes in the ventricular complex.

It is concluded that the pacemaker and conducting tissue of the heart operate essentially on aerobic energy while the myocardium is primarily anaerobic. Changes in the S-T segment of the electrocardiogram in these experiments are related, not to accumulation of metabolites nor to failure of oxidations, but to a loss of the anaerobic energy of glycogen breakdown.

Page, Irvine H.: Acetyl-Beta-Methylcholin. Observations Concerning Its Action on the Blood Pressure, Skin Temperature and the Heart, as Exhibited by the Electrocardiogram of Hypertensive Patients. Am. J. M. Sc. **189**: 55, 1935.

Mecholin (acetyl-β-methylcholin), administered subcutaneously, greatly increases the temperature of the skin of the face and trunk of patients suffering from arterial hypertension; the hands and feet usually remain almost unaffected. Administered by mouth it fails to have this action. Doses of 4 gm. taken by mouth have either no effect on the average blood pressure or a slight one only.

When administered subcutaneously, mecholin usually causes inversion of the T-waves of the electrocardiogram; this effect may be abolished by injecting atropine. Except for increasing the rate, no other characteristic action of mecholin on the heart, as observed in the electrocardiograph, was seen. The size of the heart may first be decreased and then be increased briefly, the increase occurring when the level of the blood pressure has fallen markedly.

Comparison of the clinical phenomena due to injection of mecholin with those observed in patients suffering from diencephalic epilepsy, or in patients in whom pituitrin or pilocarpin had been injected into the cerebral ventricles, demonstrates a striking similarity between them. It has been suggested that many of the effects of mecholin are due to stimulation of the diencephalic parasympathetic centers and possibly the premotor area of the cerebral cortex.

Mecholin causes most of the prominent corporal characters in the play of natural emotions to appear without being accompanied by the psychical counterpart itself.

Edeiken, Joseph, and Wolferth, Charles C.: Clinical Significance of the M or W Shaped Q-R-S Complex in Lead II of the Electrocardiogram. Am. J. M. Sc. **188**: 842, 1934.

An M or W-wave in Lead II of the electrocardiogram having the characteristics defined in this paper has not been observed in tracings of 1,077 presumably normal adults. It was seen five times (4.3 per cent) in 116 patients with the anginal syndrome. After a period of three years, four of the five patients are dead, the other incapacitated.

In 4,450 unselected electrocardiograms of hospital and clinic patients, the M or W-wave was seen in 21 tracings (0.47 per cent). Of these patients 14 are dead and six show clinical evidence of severe myocardial disease; one cannot be traced. The electrocardiograms of two of the six patients who are alive show bundle-branch block, one complete A-V dissociation, and the other three have had a coronary occlusion and are more or less incapacitated. Only two of this group have lived more than three years after the M or W-wave was first observed, and both of these are incapacitated because of pain on effort.

Of twenty-five isolated cases observed during the past two years, twenty (80 per cent) were from patients with coronary occlusion. Nine of the patients are dead; thirteen of the remainder are from the groups suspected of having had a coronary occlusion, one suffered from hypertension, and the two remaining cases are obscure and in one of these no other evidence of cardiovascular disease was found.

In most cases, the M or W-wave is probably due to an intraventricular conduction abnormality as a result of myocardial disease. Pathological changes were widespread in the three cases in which necropsy was obtained. It is possible, however, that a congenital anomaly of conduction may occasionally produce complexes of this type.

In some cases, the M or W complex has been present throughout the entire period of observation. In others, it has been relatively transient. Its appearance time following coronary occlusion is variable, the range observed in serial electrocardiograms being one day to three months.

Veal, J. Ross, and McFetridge, Elizabeth M.: Adequate Circulation in the Extremities. Arteriography as a Test for Determining Its Limits. J. A. M. A. **104**: 542, 1935.

Thirty consecutive cases of gangrene of the extremities as a result of peripheral vascular disease have been studied by means of arteriography before amputation.

It is believed that arteriography is a very much more reliable index of the limits of adequate circulation than is either the histamine reaction or the salt solution test. It is believed that the use of this test in conjunction with proper preoperative and postoperative therapy will furnish one more safeguard for the patient with gangrene of the extremities.

Allen, Edgar V., and Camp, John D.: Arteriography. J. A. M. A. 104: 618, 1935.

In the opinion of the authors, the chief value of arteriography lies not in the direction of diagnosis but in that of pathogenesis. It gives information of inestimable value regarding the minutiae of arterial disease, information which can be secured in no other way. It is to be expected that the absence or presence of organic arterial change in Raynaud's disease and the part played by disturbances in arterial circulation in scleroderma can be determined. In thromboangiitis obliterans, the part played by collateral arteries and other adjustments to impaired circulation are portrayed in a manner that leaves little to be desired. The mode of progression of the disease and the compensation for it are clearly outlined. The situation, extent, and nature of aneurysms, arteriovenous fistulas and arterial emboli can be determined accurately by arteriography.

Proger, S. H., and Korth, C.: Effect of Light Muscular Training on Patients With Heart Disease. Arch. Int. Med. 55: 204, 1935.

Six patients with rheumatic heart disease pedaled on a stationary bicycle for from one to two hours daily for a period of from five to six weeks. Two normal persons in the same age group served as controls. There were essentially no changes at rest in the pulse rate, respiratory rate (except for slowing in one case), pulmonary ventilation, and oxygen consumption.

In one patient in whom exercise had to be discontinued because of the development of hemoptysis, the arteriovenous oxygen difference at rest showed an increase, and the cardiac output a decrease, just before and after the hemoptysis. These values returned to normal within a few days after the exercise was discontinued. In the other patients the arteriovenous oxygen difference and cardiac output at rest were unchanged.

In the patients who improved with exercise, there was a slight slowing of the velocity of blood flow at rest. The vital capacity in two of the patients who improved with exercise showed a definite increase. In the normal subjects, as well as in the other patients, it remained unchanged. Breath-holding ability generally paralleled the vital capacity.

Of the three patients who showed definite improvement in their response to exercise, there was an increase in the height of P_2 in the electrocardiogram in one, and in the others an increase in the height of the T-waves. In the patients in whom hemoptysis developed, there was a slight prolongation of the P-R interval, an increase in the height of P_2, and an inversion of P_3.

There were no definite changes in the teleroentgenograms.

According to observations during exercise, the two normal subjects showed slight improvement; three patients with disease of both aortic and mitral valves showed marked improvement; one patient with only mitral disease showed no change, while another grew worse; and the only patient with an irregular heartbeat (auricular fibrillation) who also had mitral stenosis and insufficiency showed a very slight improvement.

A possible explanation for the varying responses is suggested.

In one patient, after improvement had taken place, an unexplained relapse occurred, which was overcome in a few days. In the same patient a mild infection with fever caused no change in his response to exercise immediately before and after the febrile state.

A striking parallelism is shown to exist between the pulse rate and oxygen consumption during exercise through the period of training.

Landis, Eugene M., and Hitzrot, Lewis H.: The Clinical Value of Alternate Suction and Pressure in the Treatment of Advanced Peripheral Vascular Disease. Am. J. M. Sc. **189**: 305, 1935.

The extremities of twenty-nine patients suffering from advanced peripheral vascular disease were exposed to alternate suction (−80 to −120 mm. Hg) and pressure (+40 to +80 mm. Hg) for 25 and 5 seconds, respectively. These pressure variations were used for periods of one to two hours, at first once or twice daily, then three times weekly and finally, as symptoms diminished, once weekly. Cyanosis usually diminished; symptomatic improvement was sometimes observed, however, without significant change in skin color.

The rest pain of ischemia was usually abolished during actual use of suction and pressure and gradually became less severe in the intervals between exposure to pressure variations. Lasting relief of pain was not observed in the presence of deeply extending gangrene or large sloughs.

Ulcers, enlarging or indolent under ordinary conservative treatment, usually began to heal soon after suction and pressure therapy was instituted. Intermittent claudication became, in general, milder, and exercise tolerance was slightly, but definitely, increased.

Suction and pressure therapy was of no definite, lasting service in patients with osteomyelitis, deeply extending gangrene, or large sloughs.

This form of therapy must be applied with caution, small pressure changes being used at first. The presence of acute spreading infection or encapsulated pus must be definitely ruled out before pressure variations are used.

Suction and pressure therapy, if carefully applied, appears to be worthy of clinical trial in the treatment of peripheral vascular disease even when organic obstruction has advanced to the point where arterial blood flow can no longer be increased by vasodilatation. The method may be of service by increasing local blood flow temporarily during episodes of pain or ulceration so that time is gained for the development of adequate collateral blood flow.

Lissner, Henry H., Goffin, John L. C., and Rosenfeld, Maurice H.: The Adolescent Heart. Am. J. Dis. Child. **49**: 353, 1935.

The study is based on observations on 2,840 children examined during a period of eight years. The diagnosis of adolescent heart was made in 254 children, or about 9 per cent. The subjective symptoms presented were the same as those usually considered as being present in patients with organic heart disease. These included palpitation, fatigue, dyspnea, pain, vertigo, sweating, cyanosis, epistaxis, and cough, occurring most frequently in the order mentioned. These are functional disturbances occurring during the period of adolescence and are probably produced by the unstable nervous system or by rapid physical development. The heart is greatly influenced during the rapid physiological changes associated with this period, and many functional disturbances are noted.

The solitary observation of an apical systolic murmur in the adolescent child is not sufficient evidence on which to base the diagnosis of organic heart disease. It

was noted that the murmur usually disappeared when the children were reexamined over a period of years. When the parents and the child were convinced that the symptoms were not due to organic heart disease, the child quickly became symptom-free; when the symptoms had been greatly impressed on the child, it was necessary to increase physical activity slowly and to overcome gradually the fear of symptoms.

During the adolescent period, the diagnosis of early organic heart disease is made too frequently on uncertain data. The differential diagnosis can be made only by the careful evaluation and analysis of all the data obtained, and in some instances a definite opinion should be given only after several years of careful observation.

Averbuck, Samuel H., and Friedman, William: Circulation Time in Normal Children. Am. J. Dis. Child. **49**: 361, 1935.

With the use of the saccharin method, the circulation time was determined in 100 normal children ranging in age from eight to sixteen years. The technic employed is described. The average circulation time was 8.6 seconds. The range was from 5 to 13.5 seconds. In 83 of 100 tests, the limits were from 6.5 to 10 seconds. This is shorter than the circulation time in adults, determined either by the saccharin or the sodium dehydrocholate method.

The increased circulation time in children as determined by this test is due probably to two factors: first, the actual distance to be traversed from the arm to the tongue is less than that in adults; second, the execution of the test in children induces excitement and an acceleration of the heart rate.

Von Glahn, William C., and Pappenheimer, Alwin M.: Relationship Between Rheumatic and Subacute Bacterial Endocarditis. Arch. Int. Med. **55**: 173, 1935.

Studies based on observations on a series of twenty-six consecutive cases of subacute bacterial endocarditis suggest that active rheumatic vegetations are, in persons who have had rheumatism, a necessary and practically constant prerequisite for the implantation of bacteria.

The evidence for this conclusion is summarized as follows:

1. Vegetations histologically identical with those in rheumatic endocarditis and not containing bacteria are found (a) on the same valve as the bacterial vegetations, (b) on other valves on which there are no vegetations containing bacteria, and (c) on the auricular wall.

2. Aschoff bodies in the myocardium that are taken to indicate active rheumatic disease are found in practically the same proportion of cases of subacute bacterial endocarditis as of uncomplicated rheumatic cardiac disease.

3. Types of bacterial endocarditis other than that due to nonhemolytic streptococci may be engrafted on active rheumatic vegetations. This is a cogent argument against the view that the two types of lesions are a response of different intensity to the same infective agent, unless the current views as to the histological specificity of the rheumatic reaction are dispensed with.

Faulkner, James M., Place, Edwin H., and Ohler, W. Richard: The Effect of Scarlet Fever Upon the Heart. Am. J. M. Sc. **189**: 352, 1935.

An electrocardiographic study was made of 171 cases of scarlet fever during and following the acute infection. Abnormal electrocardiograms were noted in eleven cases. The abnormalities consisted of prolongation of the P-R interval in five cases and flattening or inversion of the T-wave in six cases and did not appear before the thirteenth day from the onset of the scarlet fever in a single instance.

A follow-up study of 600 cases of scarlet fever was made from one to three years after the acute infection. It was found that seven of these individuals had developed heart disease in the interval. The type of heart disease found was indistinguishable clinically from rheumatic heart disease.

McMahon, H. E., and Pratt, J. H.: Malignant Nephrosclerosis (Malignant Hypertension). Am. J. M. Sc. **189**, 221, 1935.

The clinical and anatomical findings in a consecutive series of 100 patients with malignant nephrosclerosis, who came to autopsy, are described. Essential lesions occur in the blood vessels throughout the body, especially in the heart and kidneys.

The authors believe that malignant nephrosclerosis should not be looked upon as merely a progression of benign nephrosclerosis, but rather as a distinct and separate disease. It may occur alone or as a terminal complication of the benign disease. In the very early stages, when only the cardiovascular signs and symptoms are present, it may be impossible not only to say whether one is dealing with an early case of benign or malignant nephrosclerosis, but also it may be equally impossible to predict into which of these diseases the case will ultimately fall. As the disease progresses, the renal component becomes more and more conspicuous, and in the late stages it may be impossible to differentiate this disease from chronic glomerulonephritis. The etiology of benign and malignant nephrosclerosis has probably much in common, for one sees cases of chronic lead poisoning, pituitary basophilism, toxemias of pregnancy, and so on, which on the one hand may show benign nephrosclerosis and on the other, the much less frequent malignant disease. The course and prognosis depend not alone on the quality and quantity of the exciting agent but also in the manner in which the vessel wall responds. If the response is of a simple degenerative nature, the disease progresses slowly, the prognosis is good, and such cases are classed as benign nephrosclerosis. If the vascular response is characterized by inflammatory changes of the intima, necrosis, and hemorrhage, the course is more rapid, the prognosis is poor, and such cases are classed as malignant nephrosclerosis.

Brown, Samuel, and Alexander, Benjamin: Duroziez's Sign in Normal Subjects and in Patients With Arterial Hypertension With Special Reference to Its Relation to Capillary Pulsation and the Forward Flow of Blood During Diastole. J. Clin. Investigation **14**: 285, 1935.

The purpose of this investigation was to study in health and vascular disease the incidence of Duroziez's sign artificially produced by immersing the arm in water at 114° F.; to correlate this sign with other peripheral vascular signs such as capillary pulsation, blood pressure, and pulse pressure; to evaluate Duroziez's sign as an index of the dilatability of the peripheral vascular bed.

In sixty-three subjects with no evidence of cardiovascular disease, the incidence of Duroziez's sign decreased with advancing years. This indicates a progressive inability of the peripheral minute vessels to dilate sufficiently as age advances to provide the increased diastolic forward flow of blood necessary to produce the sign.

The incidence of the sign was studied in forty-one subjects with clinical hypertension. Compared to normal subjects of similar age groups, the incidence was in general lower, particularly with advancing age. This is in accord with the theory that arteriosclerosis is associated with arterial hypertension.

Subjects with wide pulse pressures generally showed a low incidence of Duroziez's sign of the peripheral type. This probably is due to the general coexistence of arterial and arteriosclerosis.

Capillary pulsation was studied both immediately before and after immersion of the arm in water at 114° F. Of sixty-one subjects with no evidence of vascular disease, 31 per cent exhibited it spontaneously. Of forty-one subjects with clinical hypertension, 54 per cent showed a spontaneous capillary pulsation. There was no apparent relation to age.

Capillary pulsation was particularly evident in subjects with wide pulse pressures. The greater incidence of spontaneous capillary pulsation in the hypertensive group was probably due to the greater pulse pressure generally seen in this disease.

The height of diastolic blood pressure seemed in no way to influence the incidence of spontaneous capillary pulsation except so far as the height of diastolic pressure affected the magnitude of pulse pressure.

Capillary pulsation after immersion at 114° F. was present in every case. The ages of the subjects ranged from twenty to seventy-three years. Capillary pulsation, since it was always present in the heated skin, regardless of age, cannot be used as a qualitative test of the condition of the peripheral arterioles.

Duroziez's sign produced in the manner described may be used to throw light on the geenral condition of the peripheral arterioles. According to these findings, any person under the age of thirty-five who fails to show a Duroziez's sign after immersion of the arm in water at 114° F. digresses from the physiological norm in that his functional peripheral vascular bed is relatively fixed.

Bierring, Walter L., Bone, H. C., and Lockhart, M. L.: Use of the Electrostethograph for Recording Heart Sounds. J. A. M. A. 104: 628, 1935.

The electrostethograph was designed and built by one of the authors. The principle of construction is described briefly in the article. Records of heart sounds are reproduced, illustrating the various auditory phenomena which may be heard, both murmurs and changes in sounds. The instrument offers a satisfactory method of photographing heart sounds and appears to have certain advantages over other types of recording devices. The photographic record of heart sounds is of distinct aid as a supplement to auscultatory observation as well as providing a permanent graphic record.

McEwen, Currier: Cytologic Studies on Rheumatic Fever. II. Cells of Rheumatic Exudates. J. Clin. Investigation 14: 190, 1935.

The amount, character, and cellular content of exudates from patients with rheumatic fever were studied in relation to certain clinical aspects of the disease and were compared with those of nonrheumatic exudates.

There was no obvious correlation between the amount of synovial fluid and the severity of arthritis; the number of cells per cubic millimeter ranged between 800 and 47,000, and the total number contained in the exudates tended to vary directly with the stage and severity of arthritis; the differential formula appeared to bear some direct relationship to the stage of arthritis and the age of the patient. Supravital stains revealed no cells similar to those previously described in rheumatic granulomas. Early there was a predominance of polymorphonuclear neutrophiles, with a few monocytes and undifferentiated young connective tissue cells; later there were numerous clasmatocytes containing débris and degenerating cells. Rheumatic pleural and pericardial exudates contained cells similar to those of the joints but with the addition of a few mesothelial elements. Because nonrheumatic exudates were similar in microscopical content, no specific character could be assigned to exudates in rheumatic fever.

Hitzig, William M., King, Frederick H., and Fishberg, Arthur M.: Circulation Time in Failure of the Left Side of the Heart. Arch. Int. Med. 55: 112, 1935.

In isolated failure of the left side of the heart, the arm-to-tongue circulation time is almost always prolonged, sometimes to three times the normal value. This circulation time was measured by the injection of gluside described by the authors. On the other hand, the arm-to-lung circulation time measured by a method described by one of the authors may be normal in failure of the left side of the heart despite markedly prolonged arm-to-tongue circulation time. This shows that the prolongation of the arm-to-tongue circulation time in these cases is due to slowing of the pulmonary blood flow down stream to the arterial capillaries of the lung. The prolongation of the arm-to-tongue circulation time does not always parallel the severity of the other symptoms of failure of the left side of the heart. In exceptional cases, the arm-to-tongue circulation time is within normal limits despite severe symptoms of failure of the left side of the heart.

The circulation time in failure of the left side of the heart with normal rhythm may be shortened by digitalization, furnishing further objective evidence of the utility of digitalis in many patients with this circulation disturbance. The systemic venous pressure is normal in isolated failure of the left side of the heart.

Nuzum, Franklin R., and Elliot, Albert H.: Transverse Diameter of the Heart in Patients With Hypertension, With Clinical Measurements Checked by Postmortem Studies. Arch. Int. Med. 55: 293, 1935.

The ratio of the transverse cardiac diameter to the internal diameter of the chest (Danzer ratio), as determined by orthodiagraphy, was compared with the predicted normal cardiac diameters of Hodges and Eyster in 175 persons without heart disease previously reported on and in 79 persons with arterial hypertension.

A direct correlation was found between the cardiothoracic ratio and the body weight in persons both with and without potential cardiac enlargement, such that thin persons tended to have transverse cardiac diameters less than one-half the internal diameter of the chest and obese persons had cardiac diameters greater than this by more than the experimental error of the determination.

The predicted diameters of Hodges and Eyster, while approaching more closely the actual diameters found in persons without cardiac enlargement, failed to disclose the presence of left ventricular enlargement in obese persons, but were a satisfactory guide in normal or underweight subjects. It is suggested that this is not the fault of the standard per se, but is due to the failure of left ventricular enlargement, through mechanical causes, to manifest itself by a detectable increase in the transverse diameter of the heart in obesity.

Both methods failed to demonstrate enlargement in 20.2 per cent ±8.5 of seventy-nine persons who presumably had cardiac hypertrophy.

A comparison of the incidence of cardiac enlargement, as defined by these standards, with the occurrence of left axis deviation in the electrocardiogram showed that the correlation is too indefinite to be of value in judging the relative efficacy of such measurements proposed for the detection of cardiac enlargement.

Book Reviews

KLINIK DER ERKRAUKUNGEN DES HERZMUSKELS. X FORTBILDUNG-LEHRGANG IN BAD-NAUHEIM. September 20-23, 1934. Edited by the Union of Bad-Nauheim Physicians. Theodor Steinkopff, Dresden and Leipzig, 1934.

This volume of 170 pages includes 16 lectures delivered in the annual Extension Course to Physicians given at Bad-Nauheim in the subject of cardiovascular diseases. The topic chosen for the present course is that relating to various aspects of the myocardium and its diseases. The contributions have been made by well-known students of the subjects and merit careful consideration and study.

L. A. C.

ILLUSTRATIVE ELECTROCARDIOGRAPHY. By the late Joseph H. Bainton, M.D., Attending Physician and Chief of the Cardiac Clinic, Morrisania City Hospital, and by Julius Burstein, M.D., Associate Electrocardiographer, Morrisania City Hospital, New York, N. Y. 258 pages, 100 plates. The D. Appleton-Century Co., New York and London, 1935.

The authors state that this book was planned specifically for the general practitioner. The text, for the most part, consists of legends for the illustrations. Each new subject, however, is introduced by a brief explanatory discussion to orient the uninitiated reader and prepare him to study the illustrations. The 155 electrocardiograms presented in the 100 plates have been clearly marked and arranged "in a graded sequence from normal to abnormal and from simple to more complicated phenomena." Nearly all the illustrations have been judiciously selected.

This book, in the opinion of the reviewer, offers to the general practitioner and to the casual practitioner of electrocardiography, the least painful approach to the subject thus far available. The proportion between text and illustrations is such as to avoid discouraging the not too enthusiastic seeker after knowledge, who nevertheless wishes to know something about electrocardiography. If he studies each illustration until he understands it and learns to recognize the significant features without referring to the text (not a difficult procedure and at least as interesting as solitaire), he cannot fail to emerge with a reasonable knowledge of the subject. This book is the one to be recommended to those who ask what they should read to learn something about electrocardiography.

C. C. W.

LES NÉVROSES TACHYCARDIQUES. By Dr. L. Gallavardin and Dr. A. Tourniaire. Masson & Cie., Paris, 1935, 122 pages with 24 illustrations.

In this monograph Dr. Gallavardin and Dr. Tourniaire discuss the condition known as irritable heart, effort syndrome, or neurocirculatory asthenia, which they consider to have as its most outstanding feature an instable, rapid heart rate. They point out that although the symptoms are cardiac, the heart is essentially normal and signs of cardiac failure never appear, and they repeat that the fundamental trouble is a constitutional hyperexcitability of the sympathetic nervous system. They stress the uselessness of drugs and the importance of graded exercise and reeducation in the treatment of this condition. In addition to their own observations and impressions, the authors present a survey of the literature and an extensive bibliography.

E. H.